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Agricultural Experiment Station

Bacteriology and Pathology of Sterility in Cattle

By Donald C. Beaver
With the Collaboration of W. L. Boyd and C. P. Fitch

DIVISION OF VETERINARY MEDICINE

UNIVERSITY FARM, ST. PAUL

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BACTERIOLOGY AND PATHOLOGY OF STERILITY IN CATTLE

By Donald C. Beaver

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INTRODUCTION

Sterility may be defined as the inability to produce young. (1) It may occur in either sex, but the most disastrous effects are produced when the female is no longer capable of reproducing her kind.

IMPORTANCE OF STERILITY TO AGRICULTURE

The question of continued propagation of the species in man is a sociologic one, while in the domesticated animals the economic considerations far exceed others in importance. Agriculture is a basic industry and animal husbandry bears to agriculture an inseparable relationship. The human race is concerned especially in the production of beef and milk and since the toll from sterility is greatest in cattle the economic factor of the disease must be of universal interest.

The development of a race or family of cattle is often dependent upon the successful rearing of calves from the very cows temporarily or permanently rendered sterile. The valuable purebred animal's worth is intimately related to her ability to produce calves of equally high value. When no longer capable of reproduction, her breeding can not be a source of revenue and she must be sold for beef. In the grade herd the importance of the disease to the owner lies in loss of milk production, when he must dispose of a high-producing cow for beef prices. A cow may be regarded as a machine, and must produce from the fuel (feed) she consumes, salable goods in the form of milk and calves. If this is no longer possible her value is small, depending upon market quotations.

In the male the loss from sterility is comparable, but occurs less frequently and therefore is of less concern.

We may thus sum up: Sterility is one of the most serious diseases of cattle. It strikes at the very heart of the animal industry, at times causing losses which are irreparable.

HISTORICAL RESUME

Sterility is not new, for mention has been made of it in veterinary and medical literature since the very beginnings of these branches of science. Until the brilliant research work of Lister and Pasteur led

the way to the modern and rational conception of disease, no advances were made in solving the problem. It must be admitted that altho bacteriology, pathology, and surgery have contributed much to our present knowledge, the physiologist has also added knowledge which is invaluable in dealing with the problems of sterility.

Toward the end of the nineteenth century the interest of scientific men was attracted to the field of comparative veterinary pathology and bacteriology, and much study was devoted to the diseases of the genital tract of animals. At this period the incidence of the disease seems to have increased, probably because of changed conditions in the development of our civilization, and the increased production of livestock. Infectious abortion in cattle also became more widespread and coincident with it, sterility in cattle increased. The inference is not to be drawn that infectious abortion sprang up suddenly, but rather that its importance increased because of the advances in the production of livestock. It is true also that it appeared to be more prevalent because of better recognition by an increased number of scientific observers. It is not the purpose of this thesis to discuss infectious abortion of cattle. This subject, since the time of Bang (1897) (2), has received the attention of scores of competent workers (3). The fundamental facts of infectious abortion are well described, but as infectious abortion is closely related to the increased prevalence of sterility, a passing mention should be made.

The fact that animals may be barren is stated in Genesis, Chapter 31, verse 38. In 1807 "Complete Farmer" mentions abortion as being contagious and as so regarded by farmers (4). In 1885 Nocard's investigations (5) quite clearly set forth the contagious nature of the disease, altho he did not recognize the specific infection. Woodhead, Aitken, M'Fadyean, and Campbell in 1889 (6) showed that abortion could be produced in cows by inserting into the vagina plugs of wool contaminated by the discharge of aborting cows. Until 1897, however, the etiology still remained in doubt. Through the remarkable work of Bang (2), in Denmark, the specific etiological agent was described. This is regarded without serious question as the cause of the clinical entity, "infectious abortion." The work of Bang was confirmed in England in the "Report of the Departmental Committee to Inquire into Epizoötic Abortion" (1909) (7). In America the disease was first definitely established by the identification of the organism *B. abortus* (Bang) by MacNeal and Kerr in 1910 (8). Other early workers who deserve mention for their contributions to the knowledge of infectious abortion are: Zandel, Styrl, Franck, Roloff, Brawer, and Johne. Altho not meeting with ultimate success, their studies did much in keeping the subject alive and open to further research.

In the writings of veterinary obstetritians we find the first mention of diseases leading to sterility in animals. The first veterinary work on this topic appeared in Belgium by Eberhard and Günther, 1793 (9). This was followed by the text of Skellet (10) which made its appearance in England in 1807. From this period on, publications appeared in practically every country, but for the English speaking people no real information was collected into a text until Fleming (11), in 1877, wrote his "Text Book of Veterinary Obstetrics." Hill (1882) (12), in his text, "Bovine Medicine and Surgery," devotes a short chapter to sterility in the male and female. The noted veterinarian, Dieckerhoff, in his "Lehrbuch der Speciellen Pathologie und Therapie für Thierarzte" (1888), gives excellent pathological descriptions (13) of diseases involving the genitalia of the cow. For instance, he classified metritis as acute, peracute, septic, and chronic catarrhal endometritis. Cook (14) and Awde (15) reported independently, cases of bovine endometritis in 1891. In the short paper by Awde we read, "Although I have been in practice for 15 years (1876) I can not recollect that I ever saw a case of this kind prior to the first one here recorded (1889)."

The real beginning of our knowledge concerning diseases of the genitalia of the cow dates from the time of Bang, followed by such contributors as Wall, Holth, Nielson-Sorring, Albrechtsen, Hess, Tuff, M'Fadyean, Zwick, Jensen, MacNeal, Theobald Smith, Schroeder, and Williams. Many others could be mentioned but these were pioneers in their respective countries.

To summarize: The modern conception of sterility has developed during the last twenty-five years, through advances in physiology, bacteriology, pathology, and therapeutics. The fundamental sciences have placed the veterinary gynecologist in a position to cope more successfully with the diseases of the genitalia.

DEVELOPMENT OF THE GENITAL TRACT OF THE COW

Before describing the results of the present investigation, a review of the development of the organs of the genital tract will be given. This, together with their anatomy and physiology, to be described later, is necessary for a clear understanding of pathologic changes that may occur and lead to sterility.

DEVELOPMENT OF THE UTERINE TUBES, UTERUS, AND VAGINA

Early in embryonic life, before the genital ridges have become well marked (about the second month), the ducts of Müller (Müllerian ducts or tubes) develop as two ridges near the peritoneum, near to but independent of the Wolffian ducts. They appear at first as solid rods, and later develop into definite tubes, ending blindly for a time,

then opening into the cloaca. When "hollowed out" each tube opens into the peritoneal cavity at the future fimbria of the uterine tube. Fusion later takes place caudally for a variable distance toward the anterior, thus forming a single tube of the fused portion. The latter is to become the vagina, vestibulum, *cervix uteri,* and *corpus uteri.* The anterior ends become the uterine tubes and the middle portion the *cornua uteri.* A good description of the development as occurring in the bovine species is given by Wall (16) as follows:

"The uterus, uterine tubes, and vagina are developed from a double mesodermal tube, the Müllerian tubes. These tubes merge caudally, forming the *corpus* and *cervix uteri,* and the vagina. During the fetal period the vagina opens first into the cloaca (formed by the entoderm), and then into the *sinus urogenitalis* (formed by the division of the cloaca membrane), then adjoins the ectoderm. The epithelium of all three layers of the blastoderm, the simple columnar epithelium of the entoderm and mesoderm, and the early stratified epithelium (stratified pavement epithelium) of the ectoderm then meet in the *sinus urogenitalis* (the future vestibulum). Early, even in the third month in the embryo of cattle (two investigations of embryos of 9.5 cm.), the stratified epithelium of the ectoderm seems, however, to cover the wall of the vestibulum (and of the urethra). The simple columnar epithelium of the mesoderm, bordering on the pavement epithelium of the ectoderm, which at the limit is at first double, then stratified, with a rather sharp limit, which is visible first after great microscopic enlargement. This continues until the fifth month (three examinations of embryos of respectively 18, 24, and 27 cm.), after which a slow inward growing of the ectoderm epithelium into the vagina is observed replacing it. A transformation of the mesoderm epithelium into the stratified epithelium seems not to be going on. The microscopic examinations evidently favor the hypothesis of an inward growth, as the stratified epithelium often has a staining reaction, differing from the mesoderm epithelium, but agreeing with the ectoderm epithelium (especially visible with the Unna-Pappenheim method), and further, as in the first place the connection by itself, and in the second the gradual transition from a highly stratified epithelium to a double epithelium indicate a derivation from the ectoderm epithelium. This "ectodermoisering" proceeds at different rates of speed in different individuals (five examinations of embryos of respectively 4, 4½, 4½, 8, and 9 months old). In new-born and other animals (ten examinations; two new-born calves, two calves about 2 months old; two heifers about 2 years old, and four older cows) the limit of the ectoderm epithelium was, as a rule, observed at the *os uteri externum,* or in young animals one to several centimeters behind this; but of the four older

cows the stratified epithelium in two cases was observed in the cervix and in one of these cases up to 4 cm. in front of the *os uteri externum*. It seems, therefore, as if with years the stratified epithelium spreads somewhat at the expense of the columnar epithelium, a fact which is, according to Sobotta (17), already known concerning woman. Several accouchements are considered to favor this phenomenon, which is clearly a consequence of a greater regenerative capacity of the stratified epithelium.

"In the uterine mesenchyme the differentiation between mucosa and muscular coat first makes its appearance at the end of the fourth month and the primitive carunculae begin to be visible at the same time as swelling of the mucous membrane. In the ninth month the uterine glands are first observed, first as solid then as tubular epithelium formations, growing into the mucous membrane, and the new-born calf shows a distinct layer of glands along the entire uterus, except in the carunculae."

DEVELOPMENT OF THE OVARY

At a very early stage of the mesonephros, a narrow strip of mesothelium extending along the medial surface of this structure becomes thicker and the cells become arranged in several layers. These cells become differentiated into two kinds: (1) Small cuboidal cells, with cytoplasm staining rather intensely, and (2) larger spherical cells with clearer cytoplasm and larger vesicular nuclei. The latter are the sex cells, and the whole epithelial (mesothelial) band is known as the germinal epithelium. The sex cells are destined to give rise to the sexual elements—in the female to the ova, in the male to the spermatozoa. This differentiation can not be made at first, but appears at a later period.

The cells of the germinal epithelium increase in number by mitotic division and for some time, at least, the sex cells continue to increase in number by differentiation from the small cuboidal (indifferent) cells, as indicated by the presence of intermediate stages between the two types. Their germinal epithelium soon becomes separated into two layers, (a) a superficial layer which retains its epithelial character and contains sex cells, and (b) a deeper layer composed of smaller cells which resemble those of the mesenchyme, and which give rise to a part, at least, of the stroma of the sex glands. The elevation formed by these two layers projects into the body cavity from the medial side of the mesonephros and constitutes the genital ridge. From the superficial epithelial layer, columns or cords of cells containing some of the sex cells, grow into the underlying tissue. About the end of the first month of pregnancy changes begin in the genital ridge, which differ according to whether ovaries or testicles are to be formed. The ovarian characters are: (1) The surface epithelium does not become flattened;

(2) a layer of surface epithelium, corresponding to the *tunica albuginea* of the testicle, grows between the epithelium and the deeper parts. This layer, however, is of a looser nature; (3) there is a sharp line of demarcation between the cell columns and the stroma; (4) the sex cells continue to increase in size and become more conspicuous.

During the processes of development, the anlage of the genital gland become more or less separated from the mesonephros and finally is attached only by a thin sheet of tissue—the mesovarium. At the same time it begins to grow more rapidly in thickness, becoming oval in shape.

The loose connective tissue spoken of above as corresponding to the *tunica albuginea* of the testicle, grows in between the surface epithelium and the cell columns (sex cords) and effects a more or less complete separation. The sex cords are thus pushed farther from the surface and become marked off from the surrounding stroma and constitute the so-called medullary cords. The cortex of the ovary at this stage is represented only by the surface epithelium, which is composed of several layers of cells and contains numerous sex cells in various stages of differentiation. The ovary may thus be said to be composed of two parts: (1) the *rete anlage* and (2) the *stratum germinativum*. The latter is subdivided into (a) medulla and (b) cortex.

1. The RETE CORDS develop into a group of anastomosing trabeculae which constitutes the *rete ovarii*, situated in the hilum but nearer the cephalic end of the gland. These are the homologues of the *rete testis*. The cells composing them are smaller and darker than those of the medullary cords. In some of the cords lumina appear and are lined with irregular epithelium. This stage represents the height of their development in the ovary and from this time on they atrophy, and gradually disappear.

2. (a) The MEDULLARY CORDS are composed of small epithelial cells and a large number of sex cells. These are surrounded by a stroma. During fetal life they give rise to primary avorian follicles, later they degenerate and finally disappear.

(b) The CORTEX of the ovary at first consists of several layers of small, darkly staining cells, among which are many large, clearer, sex cells, or primitive ova. From the epithelium, masses or cords of cells grow into the underlying tissue, carrying with them some of the primitive ova. These masses are known as Pflüger's egg cords. The epithelial cells give rise to the follicular cells and are seen constantly undergoing mitotic division. The primitive ova increase in size and their nuclei show a chromatic network.

The egg cords break up and become separated from the surface epithelium, so that a single ovum is surrounded by a single layer of epithelial cells. These constitute the primary Graafian follicles. The formation of egg cords is usually completed at birth but in rare instances continues for a short time after birth. The stroma increases so that the egg cords become separated by a considerable amount of connective tissue. Their germinal epithelium becomes reduced to a single layer of epithelial cells.

Each primary ovarian follicle, containing a primitive ovum, is composed of a single layer of flat or cuboidal cells, plus a layer of stroma, which gives rise to the *theca folliculi.* After the follicular epithelium has become several layers thick, a fluid substance known as the *liquor folliculi,* and probably derived from these cells, is secreted around the cells. As the follicle enlarges these pools coalesce and form a single large pool, lying in the center of the follicle. Thus the epithelial cells are crowded toward the outside, where they form a layer several cells in thickness, known as the *stratum granulosum.* The ovum is likewise crowded toward the periphery of the follicle. The little elevation of the *stratum granulosum* in which the ovum is imbedded is known as the *cumulus oöphorus.* As the follicles approach maturity they gradually enlarge, pushing through the cortex until the *tunica albuginea* is reached. Various views are held in regard to the size that the follicle may acquire. In woman the size averages 5 mm., but varies (18). In the cow, Albrechtsen (19) states that "A follicle is regarded as mature when it reaches a diameter of 10-15 mm." According to Hess (20), 10-14 mm.

It must be borne in mind that development of the follicles is slow and they do not reach maturity until the age of puberty. In heifers this may be the 5th, 6th, 7th, or 9th month, but according to Fleming (21) the age of puberty is from 12 to 18 months. Saint Cyr (21) gives the age of puberty in the bovine species at from 12 to 14 months. De Bruin (22) states that on the average the cow reaches puberty at 10 months of age. When the follicle reaches maturity, other conditions being favorable, it ruptures at the surface of the ovary and the ovum is set free. It has been estimated that from 10,000 to 36,000 primitive ova appear in each human ovary, a vast number of which, it may be seen, never reach maturity. The number of ova in the ovary of the cow at birth varies considerably. Heitz (23) estimated the number to be 3800, while according to Käpelli's (24) investigations the number varies within wide limits (6740 to 297,668).

ANATOMY OF THE GENITAL TRACT OF THE COW

1. BONES OF THE PELVIS

The PELVIC GIRDLE (*Cingulum extremitas pelvinae*) consists of the *ossa coxarum,* which unite ventrally in the symphysis pelvis and articulate with the sacrum dorsally.

The *os coxae* is the largest of the flat bones. It is made up of three parts, the ileum, the ischium, and the pubis, which meet to form the acetabulum, a large cotyloid cavity for articulation with the head of the femur. These parts are fused at about 1 year of age.

The pelvic inlet is elliptical and oblique. In a cow of medium size the conjugate diameter is 23 to 24 cm. and the transverse diameter about 18 cm.

The LIGAMENTS of the pelvic girdle constitute important structures in the support of the generative organs. These are (1) dorsal sacro-iliac ligament, a strong band which is attached to the *tuber sacrale* and the summits of the sacral spines; (2) the lateral sacro-iliac ligament, a triangular thick sheet which is attached in front to the *tuber sacrale* and adjacent part of the median border of the ilium, above the great sciatic notch, and below to the lateral border of the sacrum; (3) the sacro-sciatic ligament, an extensive quadrilateral sheet which completes the lateral pelvic wall. Its dorsal border is attached to the border of the sacrum and the transverse processes of the first and second coccygeal vertebrae. Its ventral border is attached to the superior ischiatic spine and *tuber ischii.* Between these it bridges over the lateral border of the ischium and completes the lesser sciatic foramen. The anterior border is concave and completes the greater sciatic foramen.

2. VAGINA

The VAGINA is the passage which extends nearly horizontally through the pelvic cavity from the neck of the uterus to the vulva. In the non-pregnant animal its length is 20-25 cm. In pregnancy its length increases to 30 cm. or more. The retro-peritoneal pouch of peritoneum extends backward about 12 cm. on the dorsal surface; ventrally the serous coat extends backward but 5 cm. In the ventral wall of the vagina, between the muscular and mucous coats there are commonly two remnants of the Wolffian duct, the canals of Gärtner. When well developed (or occasionally cystic) they may attain a diameter of 3 mm., and may be traced forward to the anterior portion of the vagina or even farther along the broad ligaments toward the ovary. They have an opening posteriorly toward the external urethral orifice. Röder states, according to Sisson (25), that the right canal was absent in 52 per cent of cases, the left in only 22 per cent.

The VULVA has thick, wrinkled labia, and both commissures are acute; the ventral one is pointed, and has on it a number of long hairs. It lies about 5 cm. behind and about the same distance below the ischial arch. The external urethral orifice is 10 to 12 cm. from the ventral commissure. Beneath the opening there is a blind pouch, the suburethral diverticulum, which is about 3 cm. long and into which the finger may be easily inserted. The two *glandulae vestibulares majores* (glands of Bartholin), are situated in the lateral walls of the vulva, under the *constrictor vulvae*. They are about 3 cm. long and about 1.5 cm. wide. Each has two or three ducts opening into a small pouch of the mucous membrane. This opens just above the floor of the vulva about 3 to 4 cm. lateral to and behind the external urethral orifice. The gland is lobulated, being separated into lobules by connective tissue and muscular bands. The *glandulae vestibulares minores* occur along the median ventral groove. Numerous lymph nodes are present in the mucosa and may be large enough to cause slight prominences. The clitoris has a very short crura, but the body is 10-12 cm. long and is flexuous. Only the pointed end of the gland can be seen in the ventral commissure of the vulva.

The wall of the vagina is composed from within outward of a mucous membrane, a muscular and a fibrous coat. The epithelium is stratified ectodermal epithelium, which in older animals always extends forward, covering the *os uteri externum,* where transition occurs to the columnar epithelium as seen in the uterus. The mucous membrane has no mucus glands, the mucus seen on it supposedly being derived from the cervix and uterus. The muscular coat is composed of fibers having a longitudinal direction. The muscle is unstriped. The fibrous coat is dense and thick and is composed in part of areolar tissue. The peritoneum is reflected over it in places, forming a serous coat.

The vagina is richly supplied with blood vessels and nerves. The arteries are derived from the branches of the internal iliac, viz.: the vaginal, internal pudic, and uterine. The veins correspond. There is a close network of lymphatics throughout the mucous membrane, these draining toward the internal iliac nodes. The nerves are derived from the sympathetic, through the pelvic plexus.

3. UTERUS

The UTERUS lies almost entirely within the abdominal cavity in the adult. It is a uterus bicornis, the body being relatively short. The cornua are relatively long. As a rule the body is less than 4 cm. in length but may occasionally be longer. The muscular and fibrous coats of the inner portions of the cornua walls are connected for a considerable distance anterior to the body, and are invested by a single peritoneal

investment. For this reason, upon external examination the cornua appears to be 15-18 cm. in length, while in reality the length is 35 cm. Their breadth at the body is about 3 cm. The cornua taper gradually toward the uterine tubes where the size is gradually carried out without an abrupt transition from uterus to tube. The free part of the horn curves at first forward, upward, and outward, and then turns backward and downward, forming a spiral coil. In the non-gravid organ the mucous surfaces of the uterine walls are normally in contact with each other. Posteriorly the cavity of the uterus is continuous with the vagina, through the cervical canal.

The CERVICAL CANAL (*canalis cervicis*) is a tortuous canal about 7 cm. or more in length. According to Sisson (25) the length is 10 cm. It can easily be seen that it is dependent for its length upon the length of the *cervix uteri.*

The CERVIX UTERI consists of a constricted portion of the uterus, the circular muscle fibers being more numerous than in the uterus. The walls are very dense (muscular and fibrous), and measure about 3 cm. in thickness. The lumen (cervical canal) in the bovine species is spiral-shaped. It is difficult to dilate. The walls on either side are in quite close apposition except in estrum and during and following parturition. Posteriorly a portion of the cervix projects into the vagina for a distance of 3-5 cm. in the form of a truncated cone the diameter of which varies greatly, but according to Williams (26) approximates its longitudinal dimensions. The projection into the vagina is properly called *portio vaginalis uteri,* or *os uteri externum.* The tip presents posteriorly many longitudinal converging folds in its mucous membrane which remind one of a radiating flower. The cervix anteriorly joins the *corpus uteri* and is called at that point the *os uteri internum.*

Microscopically the uterine wall is seen to be made up of three coats: (1) mucosa (the endometrium), (2) muscularis (the myometrium), and (3) serosa (the perimetrium). There is no sub-mucosa. In thickness the mucosa ranges from 1.5 to 4 mm. The surface is lined by high columnar epithelium which in the cornua is 30-50 microns in thickness, and in the body about 20 microns. The mucosa of the bovine uterus is especially elaborated in parts for the accomodation of the fetus. To these parts the name carunculae, or maternal cotyledons, is applied. It is this specialized formation, especially in the bovine uterus, which forms the maternal placenta of pregnancy and in which connections between the fetus and mother develop. Thus we may divide the mucosa into two parts: (1) The carunculae, (2) the gland mucosa.

1. CARUNCULAE are oval prominences, about 100 in number, either irregularly scattered over the surface or arranged in rows. They are

covered by the ordinary uterine columnar epithelium, and in the virgin uterus form little swellings over the surface of the mucosa. They are 3 cm. in diameter and 1.5 in depth. Beneath the epthelium are found no glands, but numerous connective tissue cells (old and young), fibers, and a few scattered lymphocytes throughout the connective tissue reticulum. Numerous large and small vessels are also noted not a great distance from the epithelial surface. The carunculae do not reach the muscular coat, but only approximate it. There are usually in the area above the muscular coat a few uterine glands which open at the sides of the carunculae, never on their surface. In pregnancy the carunculae undergo a remarkable evolution, seemingly an embryological development, similar to that seen in the uterine glands. Wall (27) considers them as depots of embryonal tissues of great vegetative power. He states that they appear as epithelium and connective tissue with vessels, which develop in pregnancy and undergo involution after parturition. "In pregnancy these carunculae attain the weight of 200 gr., with dimensions up to 9 cm. (length) by 7 cm. (breadth), by 6 cm (thickness), with a stem about 6 cm. long and 3 cm. broad, growing thinner at the caruncula." They present a convex inner surface and are on stalks instead of being sessile. The carunculae in the pregnant uterus show per square cm. from 10 to 30 crypts, often 10 cm. deep, resembling in form a three-, four-, or five-edged, obtuse pyramid, narrowing irregularly toward the peritoneum (outside). Inward (nearest the embryo) they are 0.3 mm., but at the bottom only about 0.1 mm. in width (27). The surface has a deep sponge appearance due to this development. The walls of the crypts are composed of closely arranged fibers and rather numerous fibroblasts, and a few scattered lymphocytes and polymorphonuclear leukocytes. The epithelium of the crypts is simple, low cuboidal, with rather numerous emigrating leukocytes. At the bottom there is a dense, highly vascular, connective tissue. Into the carunculae crypts the chorionic villi of pregnancy grow, one growing into each crypt and branching like a tree to fill the various niches.

After pregnancy has ended the carunculae undergo involution, corresponding to the involution of the entire organ. The reduction in size is rapid, so much so that within three days after parturition they are only one-fifth the volume of those of the last month of pregnancy. Hemorrhages and hyaline degeneration can be observed in the carunculae stromata, together with necrobiosis of the cells (27). The necrobiosis begins at the lumen of the uterus and goes outward (toward the peritoneum). Occasionally blood vessels may show white thrombi. In the crypts the pavement epithelium shows defects. Cells are observed among which are red blood corpuscles, lymphocytes, polymorphonuclear

leukocytes, and remains of chorionic villi which show a granular degeneration. The next step in the involution begins about the fifth day after parturition and ends between the tenth and fourteenth days, during which time the dropping off of the carunculae occurs, as described by Hilty and Sommer (28). It may thus be seen that the loss of the carunculae with considerable mucous membrane, corresponds to the sloughing of the decidua in deciduate animals (as in the primates). The whole caruncula rarely sloughs off, and when it does, only in small portions. The necrotic material passses away in the lochial fluid. After the birth of one calf the carunculae remain larger than in the virgin uterus, reducing in volume to 10 mm. in length (diameter) and 4 to 5 mm. in thickness. They are often slightly depressed at the center. They show in this state a loosely reticular connective tissue, supporting the normal high uterine epithelium of columnar type, through which may be seen fibroblasts, solitary lymphocytes, and in its deeper portion, many large vessels. These have thick walls and fine lumina, some showing hyaline degeneration of the intima and thickened media.

2. The GLAND MUCOSA has as its principal difference from the carunculae the presence of numerous uterine glands. It consists of two layers, (a) an inner layer, called by Ellenberger (29) *stratum cellulare*. This is about 0.5 mm. in thickness. In this area one finds numerous fibroblasts, scattered lymphocytes, a few polymorphonuclear leukocytes, and a finely arranged network of connective tissue through which numerous capillaries may be found. (b) The outer layer is thicker, contains a greater number of connective tissue fibers and fewer wandering and lymphoid cells, but has in connection with it simple convoluted tubular uterine glands. No sub-mucosa exists. The simple columnar epithelium of the uterine glands is without cilia, which generally holds true for the surface epithelium of the mucosa. In gravid and involuted uteri, however, there may be ciliated processes projecting into the lumen, which Wall (28) regards as being only the fibrinous product of secretion. Wall's figures are here quoted for the number of tubuli at different stages in the gravid and non-gravid uterus, "The maiden uterus in two-months or older heifers, calculated on four uteri, shows 600 to 700 cross-cut tubuli per centimeter of mucous membrane in sections of 10 microns. These tubuli have an average diameter of 17 microns. The gravid uterus (three uteri) shows an average number of 100 to 150 tubuli with a diameter of about 150 microns. Within three days *post partum* there can be counted 100 to 200 tubuli with a diameter of 50 microns. The involuted uterus (six uteri) 300 to 1000, on an average about 700 tubuli—with a diameter of about 17 microns."

It may thus be seen that the tubuli grow very large during pregnancy, but regain more or less of their former size in the involuted uterus.

The muscular coat is composed of an inner circular layer of unstriated muscle, and an outer longitudinal layer, beneath the serosa. These fibers are much enlarged in the gravid state of the uterus. The fibers interlace closely, are disposed in bundles or layers, and are intermixed with areolar tissue, containing a large number of blood vessels, lymphatics, and nerves. The areolar tissue is more abundant near the outer surface.

The external layer of the muscular coat lies directly beneath the serosa. A large number of muscle bundles begin as longitudinal bands in the cervix and are continued through the cornua and eventually pass off into the uterine tubes. The inner muscular layer and the point of ramification of the blood vessels before they pass into the mucosa serve to mark off the mucous membrane from the muscular coat proper. The width of the muscular coat is from 1.5 to 6 mm.

The serosa is a special investment of the peritoneum, consisting of a layer of flattened endothelial cells, supported by a thin elastic membrane. It shows but few alterations in the evolution and involution of the uterus.

In structure the cervix is similar to the uterus. The mucosa is free of glands (in this respect differing from the human cervix) and is much plaited by longitudinal folds, so that in cross-section it appears as a mural crown. The mucosa of the cervical canal is also thrown into transverse circular rugae, three or four such folds being present. The epithelium is for the most part single and low columnar, except that of the *os uteri externum* (*portio vaginalis uteri*) which is covered by a stratified ectodermal epithelium, as seen in the vagina. "In old cows this may spread forward 4 cm. in front of the *os uteri externum* by "ectodermoisering." Altho no cervical glands exist, its epithelium, through the presence of goblet cells, secretes a mucus, having an important rôle to play in the formation of the seal in pregnancy. The folding of the epithelium adds much surface for mucous secretion. The muscular coat is very dense and thick, the circular fibers being much more abundant than in the body or horns of the uterus. The serosa, where existing, is similar to that seen at other portions, previously described.

The arteries of the uterus and cervix are derived from the uterine and the uterine branch of the utero-ovarian, and the internal pudic. Veins accompany the arteries. Lymphatics are numerous and drain toward the internal iliac and lumbar lymph nodes. The nerves are derived from the pelvic and uterine plexuses.

4. UTERINE TUBES

The ovaries are regarded as glands for the production of ova, and the UTERINE TUBES (*tuba uterina*) represent their ducts. They do not start immediately at the ovaries, but open up into the peritoneal cavity near the ovary where they present a small orifice surrounded by their fimbria. The fimbria comes into close relationship with the ovary and may be attached at one end. When the ova are discharged they fall upon the fimbria and are transported through the lumen of the uterine tube to the uterus. At the uterine end of the tube its communication is reduced somewhat in size, forming the isthmus. Between the isthmus and the fimbriated extremity is the ampulla (near the fimbriated end).

In the bovine species, the tube is thin and tortuous and is supported by a specialized peritoneal reflection. Its entire length is from 21 to 28 cm. At the isthmus the thickness varies from 0.8 to 1 mm. and at the ampulla is from 3 to 5 mm. in diameter (29).

The uterine tube shows, microscopically, three layers: The *tunica mucosa,* the *tunica muscularis,* and the *tunica serosa.* The mucosa is supported by a *tunica propria* or basal membrane and is thrown up into folds, projecting for a greater or lesser distance into the lumen of the tube. In the bovine species these plicae vary in number from 20 to 40. The epithelium, which is supported by the stroma of the *tunica propria,* is simple (or pseudostratified), ciliated, and high columnar in type. It covers the mucosa throughout the length of the tube. The *tunica muscularia* is composed of both circular and longitudinal fibers of plain muscle. The circular layer is much the stronger and is located nearer the lumen of the tube. The longitudinal fibers are seen external to the circular and are less developed. The muscularis is strongest near the uterine end of the tube. The serosa is a specially reflected portion of the peritoneum (serous mesothelium) which covers the external portion of the tube, forming its *tunica serosa.*

The ARTERIES are derived from the utero-ovarian, and the veins are satellites of the arteries. The lymphatic vessels pass with the ovarian vessels to the lumbar lymph nodes. The nerves come from the sympathetic, renal, and aortic plexuses.

5. OVARIES

The OVARIES are two small, oval, somewhat solid looking bodies, lying one on each side of the pelvis, and projecting into the peritoneal cavity at the posterior part of the broad ligament, which is itself formed by a fold of peritoneum. During sexual life a number of clear vesicles can be seen near the surface of the ovary, sometimes even projecting beyond the surface. These are the ripe or ripening Graafian follicles.

There may also be seen occasionally one or more yellow masses imbedded in the ovary, the *corpora lutea.* These may project slightly from the surface of the ovary, in the form of a small rounded elevation. Their dimensions on the average are 1½ to 2½ cm. in length 1⅓ to 2⅔ cm. in breadth, 1⅓ to 1½ cm. in thickness, with a weight of from 10 to 15 grams. The right ovary is slightly larger than the left (30).

Each ovary is formed of a solid mass of fibrous looking tissue, which contains between its fibers very many elongated cells, like those of embryonic fibrous tissue. The stroma is more condensed near the surface where it forms the *tunica albuginea.* The ovary projects into the peritoneal cavity, but is not actually covered by a serous membrane. The peritoneum ceases abruptly at the attachment to the broad ligament. Along this line of attachment (hilum), blood vessels and nerves enter and leave the ovary. In this location frequently are seen a large number of interstitial cells, much like those seen in the testis. Similar cells may occur scattered in groups about the stroma, but do not seem to be numerous in the bovine ovary. A layer of short, clear, columnar epithelial cells (the germinal epithelium) covers the entire clear surface of the ovary. Primitive ova may occur among them. Here and there, especially in the young animal, the epithelium is thickened and dips into the stroma of the ovary. These have been described in the embryology of the ovary as Pflügers egg tubes (or cords). In the development of the ovary these cords become broken up into islands of epithelial cells, from which the Graafian follicles arise. Imbedded in all parts of the cortical stroma, except near the hilum, are a large number of spherical or ovoid vesicles, each containing an ovum, together with other cells. These vesicles are the Graafian follicles. They are of all sizes ranging from the size of the ovum, and entirely microscopic, to 15 mm. in diameter. The smallest Graafian follicles contain only a small ovum and a single layer of epithelial cells surrounding it. The largest contain an ovum of mature size (about 0.2 mm. in diameter) surrounded by a considerable mass of epithelial cells, known as the *cumulus oöphorus,* by which it is attached to the wall of the follicle. Layers of the same cells line the wall continuously, and constitute the *stratum granulosum.* The wall itself is fibrous and known as the *theca folliculi.* The large follicles are distended with a clear, straw-colored fluid, the *liquor folliculi.* As the fluid accumulates the follicles project from the surface as little convex, translucent elevations. It is at this point that the follicle eventually bursts, liberating the ovum surrounded by its *cumulus oöphorus.* The *stratum granulosum* remains *in situ* and undergoes proliferation, developing into the epithelial tissue

of the *corpus luteum.* The smallest Graafian follicles (primary follicles) are found near the surface of the ovary, in the so-called cortical layer. As the follicles develop they sink into the stroma, and as they become enlarged through the elaboration of their *liquor folliculi* (probably secreted by the *membrana granulosa*) again approach the surface. Many follicles never go beyond the primary follicle stage but after a time undergo a degenerative change by either atrophy or atresia of the follicle. The *theca folliculi* undergoes growth and organization, finally replacing the follicle. These are known as atretic follicles. The ova are large spherical cells with clear nuclei and large nucleoli. They are enveloped by a clear membrane known as the *zona pellucida.* The ovum is composed of clear cytoplasm, the vitellus, a large vesicular nucleus, the germinal vesicle, within which is a single dark staining nucleolus, or germinal spot. The cytoplasm (vitellus or yolk) contains many granules, especially near the central part. The nucleus (germinal vesicle of Purkinje) measures about 0.05 mm. in diameter. Following the rupture of the Graafian follicle and the escape of the ovum, there is considerable hemorrhage. This blood clots in the former cavity of the follicle and gives rise to the *corpus rubrum.* The follicular wall begins, almost immediately, to hypertrophy and is thrown up into folds or plaits. The greater part of the hypertrophy is from a thickening and proliferation of the epithelial cells of the *stratum granulosum,* followed by inward growth of vascular processes chiefly from the *theca folliculi.* The *corpus rubrum* undergoes dissolusion and absorption before this advancing growth, which when completed is known as the *corpus luteum.* The cells of the *corpus luteum* are known as lutein cells, and grossly appear to be yellow. The pigment is for the most part carotin with small amounts of xanthophil (31).

The *corpus luteum* is at first sharply marked off from the surrounding ovarian stroma, by the *theca folliculi.* After a time it becomes less sharply differentiated from the stroma. The lutein cells undergo absorption, and connective tissue replacement which later becomes contracted and subjected to hyaline changes. Thus in ovaries of aged animals white scars are prominent throughout the stroma, which often even cause an irregular scarring of the ovarian surface. These remains of the *corpora lutea* are known as *corpora albicantia* or simple sclerotic *corpora lutea.*

The arteries are derived from the ovarian arteries which are large and flexuous and reach the ovary by passing between the layers of the mesovarium. Veins are large and numerous. Lymphatics drain toward the lumbar nodes. Nerves are derived from the sympathetic system through the renal and aortic plexuses. The vessels enter the ovary at the hilum.

6. ATTACHMENTS OF THE GENITAL ORGANS

The body and cornua of the uterus are attached to the abdominal and pelvic walls by two extensive peritoneal folds, the broad ligaments (*ligamentum lata uteri*). These extend on either side from the upper part of the flanks, about a hand's breadth below the level of the *tuber coxae*, to the dorsal border of the cornua and the lateral margins of the body of the uterus. They contain the blood vessels, lymphatics, and nerves of the uterus and ovaries, connective tissue, and a considerable amount of unstriped muscle which is continuous with the smooth muscle of the uterus. The ureters are situated along their parietal margins. The lateral layer of each gives off a fold, the round ligaments of the uterus (*ligamentum teres uteri*), which blend with the parietal peritoneum, and can be distinctly traced to the vicinity of the abdominal inguinal ring. The anterior extremity of this ligament is situated above the extremity of the cornu, and forms a long, round appendix. It contains muscle tissue, vessels, and nerves, and is the homologue of the *gubernaculum testis*. The anterior part of the neck is continuous with the vagina, and thus has a more fixed position than the rest of the organ.

DEVELOPMENT AND STRUCTURE OF THE FETAL MEMBRANES

Fertilization of the ovum usually occurs in the isthmus of the uterine tube, after which the ovum descends into the uterus, sometimes during the first week of pregnancy, still surrounded by its *zona pellucida*.

Upon arrival of the fertilized ovum in the uterus, the condition of that organ is typical of that of the unimpregnated organ (to be described later). The glands contain very little secretion and no trace of blood or debris. The stroma cells increase in number and become more dense, leukocytes begin to invade the epithelium. The ovum soon becomes implanted in the uterine wall, and the fetal membranes develop about it. A destruction of the uterine epithelium begins about this time (18 days) over the carunculae, and extends to all parts of the uterus that are in contact with the growing embryo. Regeneration of the epithelium over the carunculae does not occur until after parturition, while over the intercotyledonary areas (the gland mucosa) regeneration takes place about the third month of pregnancy.

About the fertilized ovum there develop, soon after conception, certain appendages. These are: (1) The chorion, with the *placenta fetalis*, (2) the amnion, and (3) the allantois. These serve to protect the fetus and to carry maternal nourishment to it.

"The CHORION (or vascular membrane) is the outer envelope surrounding the foetus and the two inner membranes, and adapts itself closely to the outer surface of the mucous membrane of the uterus."

(22) Its development permits it to extend into the non-impregnated horn and *corpus uteri*. On its external surface there are tufts of villi which constitute the fetal cotyledonous placenta. The chorion arises partly from the superficial layer of the morula (ectoderm) and partly from the embryonic parietal mesoderm, which develops later. The trophectoderm forms the outer layer of the blastodermic vesicle, which internally is made up of a mass of cells. The trophectoderm forms the primitive ectodermal layer of the chorion, which is composed of a single layer of cuboidal epithelial cells, and several ovoid binucleated cells. The former probably correspond to Langerhan's layer of the human chorion, the latter to the syncytium. These represent the growing elements of the chorion, the chorionic villi. The mesoderm gives rise to a connective tissue stroma supporting the ectodermal layer, which also accompanies the trophoblast of the villus, forming a connective tissue core, or supporting stroma. The villi grow into the swollen carunculae and this union constitutes the fetal and maternal placenta. The exchange of nutritive material takes place between the fetal placenta and the mother through absorption and imbibition of maternal juices. There is no direct communication between the maternal and fetal circulations. The chorionic villi approximate the large vessels of the carunculae and obtain for the fetus materials essential to its life. The fetal blood vessels follow the stroma of the chorion and thus (as they arise from the allantois) the blood-borne waste products of fetal metabolism are also eliminated and taken up by the maternal uterine circulation. In ruminants the chorion is united to the amnion and allantois over the middle of its inner surface, by loose gelatinous connective tissue. On the surface of the cotyledons of the cow is found a fluid in the nature of an emulsion (uterine milk). It is a whitish or reddish emulsion of alkaline or neutral reaction, with a specific gravity of 1.036. Gamgee (22) found in 1000 parts of uterine milk: Water 879.1 parts, solids 120.9 parts, the latter being represented by albumin (with the cells) 104 parts; alkaline albuminates, 1.6 parts; fats 12.33 parts; organic salts 3.74 parts; also some creatin, creatinin, and xanthin. Colin (22) regarded it as a post-mortem product of decomposition, while other experimenters regard it as possessing an important nutritive function.

The AMNION begins to develop as soon as segmentation has been completed and the ovum has reached the uterus. It appears at approximately the end of the second week of pregnancy. The development of the amnion has been traced to the external layer of the blastoderm. It begins at the umbilicus and surrounds the fetus like a sac, enclosing it entirely except at the point of origin, where it takes part in the formation of the umbilicus. It is a thin, double membrane of little resistance. In ruminants the inner surface is studded with little

yellow projecting points, called by Claude Bernard (22), "plaques glycogenique," for they are composed of glandular tissue capable of producing glycogen. In this respect it is held that this function replaces the function of the fetal liver, until that organ is developed (Joulin, St. Cyr, and Violet in "Traite d' Obsteterique"). Lecoq (22) holds that they are simply changed parts of the fetal skin. They are most numerous about the amniotic portion of the umbilicus. The external surface of the amnion is partly in contact with the allantois laterally and at the back of the fetus with the face of the chorion. The inner of the two membranes, previously mentioned, constitutes the true amnion, while the external one forms the external or false amnion, which by fusion replaces the prochorion, thus forming the primitive chorion. Later when the allantois grows out it blends with it to form the permanent or allantoic chorion. This outer or false amnion is merely a portion of the external wall of the blastodermic vesicle, without having had its relations changed exteriorly. The space between the amnion and the fetus constitutes the amniotic cavity and is distended with a clear straw-colored fluid. It is oval in shape with a depression at the umbilicus, thus giving to it a kidney or bean shape. As it becomes filled with fluid and enlarges it invests the vitelline stalk and allantoic cord in its passage through the cavity. In the latter part of pregnancy the fluid becomes mucoid, opalescent, and stringy, and may contain fetal feces (meconium), giving it a brownish tinge. The amount of amniotic fluid at birth averages 4 kg. It serves a mechanical function, protecting against injury and lubricating the vagina during parturition.

The ALLANTOIS arises as an invagination from the hind gut, just posterior to the vitelline duct, and grows outward and backward between the two amniotic layers (or if considered as by some authors, between the chorion and amnion). It is a continuation of the urachus and is sacular in shape, from which it receives its name, allantois (Gr. sausage). The urachus forms a tube for communication between the allantois and urinary bladder of the fetus. The external face of the allantois rests on the internal face of the chorion. When the allantois is isolated and emptied it is seen by inflation to be a bicornual, irregular, cylindrical sac, the head of the fetus lying in the shorter cornu, the posterior extremities in the larger. The allantoic sac contains the allantoic fluid (the fetal urine), which gradually accumulates. It is a whitish foamy, thin fluid of neutral reaction, which later in pregnancy becomes yellow or brownish. Near the end of pregnancy it amounts to from 8 to 15¼ liters. Robin (22) has proved the absence of glucose, oxalates, albumin, mucus, allantoidin in the allantoic fluid. The allantois is important in transporting the fetal blood vessels to the chorion, and to the chorionic villi of the placenta, where the transference

of maternal nourishment to the fetus occurs. It also acts as a reservoir of fetal urine.

Other important appendages are the vitelline or *yolk stalk,* supplying nutrition to the developing embryo until maternal connections can be obtained. It is not of importance beyond this. It arises from the primitive gut. The umbilical cord is composed of the urachus, two umbilical arteries, two umbilical veins, and the remains of the yolk stalk. All these are imbedded in a gelatinous mass, "Wharton's gelatin" or jelly. The sheath of the umbilical cord is formed from folds or invaginations of the amnion. The urachus carries the fetal urine to the allantois. The umbilical arteries supply the fetal membranes and as previously stated, through their circulating blood exchange fetal katabolic products for maternal nutritive products, in the placenta.

PHYSIOLOGY OF REPRODUCTION

THE ESTRUS CYCLE

The cycle of events leading to estrum (or heat) is known as the *diestrous cycle.* The cycle is usually divided into four states: (1) *proestrum* (period of growth and congestion, followed by the period of destruction), (2) *estrum* (beginning period of recuperation—"heat"), (3) *metestrum* (period of recuperation), (4) *diestrum* (period of rest). If conception does not occur at any estrus period during the sexual season, a prolonged period of rest may follow. This is known as the anestrous period. The latter is ordinarily shown only by certain species of animals having definite breeding seasons. The complete cycle of events, including anestrum, is known as the anestrous cycle.

The periods of proestrum and estrum are commonly referred to as the "heat period." As a matter of fact there is a marked physiological difference in these two periods, *proestrum* corresponding to *menstruation* in the human female, in which there is an increased activity of the uterine glands resulting in congestion of the uterus. Frequently at this time bloody or clear mucus containing polymorphonuclear leukocytes and other white blood cells can be seen coming from the glands, followed by epithelial destruction and bleeding. The amount of blood is slight in the cow, but is commonly seen in the vagina. In sheep, where careful studies have been made, bleeding is a well established fact. This corresponds to the menstruation of the human female but is much less marked. The period lasts from 2 to 4 days as a rule. The *proestrum* is a process preparing the uterus for implantation of the ovum in its wall and corresponding as it does to menstruation probably does not occur as Williams states (26), based on clinical evidence, after the *estrum,* but before, as was pointed out by Heape (32)

and later by Marshall (33). Any other conclusion would make it necessary to change our entire conception of the physiology of *proestrum* or menstruation.

Proestrum is followed by *estrum* which is of very short duration. It marks the climax of the estrous cycle. At this time the female is willing to take the male and fruitful coition is possible. The uterus is in the beginning of recuperation, the glands are less active, hyperemia subsides and healing has commenced. Large numbers of leukocytes can be seen in the stroma. Some are phagocytic for the cellular detritis and blood pigment remaining from the proestrus.

If conception occurs, this period is followed by the *period of gestation*, which in the bovine species has an average duration of 275 days.

On the other hand, should conception not occur during estrus, the latter is succeeded by a short *metestrum*, during which activity of the generative organs subsides and they gradually return to normal.

In some animals the *metestrum* may be succeeded by a long period of quiesence, the *anestrum*, while in others it is followed simply by a short period of rest. This interval is known as the *diestrum*. Following this period of rest, *proestrum* (period of growth and congestion followed by period of destruction) again begins, and the diestrous cycle is complete. It is probable that the uterine changes do not take place abruptly, but that each day marks certain differences in the progress of the cycle. The latter has been well studied in the human female and in the apes, where a menstruation similar to that in woman occurs. In primates the cycle may be divided into four stages:

(1) The stage of construction
(2) The stage of destruction
(3) The stage of repair
(4) The stage of quiescence

The completion of the diestrous cycle in cattle, according to Ellenberger (63) varies from two to four weeks. Wallace (57) states that in summer estrus occurs among cattle every nineteen days, but in winter every twenty-one or twenty-two days. After parturition the cow usually appears to be in heat again within four or five weeks. The domestic cow is polyestrous, having several recurrent breeding periods at more or less regular intervals each year.

THE OVARIAN FACTOR IN REPRODUCTION

Through continued experimental evidence it has been adduced that the diestrous cycle is definitely controlled through the activity of the ovary. Heat and menstruation are brought about by the elaboration of some sort of chemical substance or hormone, having its source in the ovarian tissue. This so-called internal secretion, not only controls the functional activity of the uterus, but also has to do with the

development of the mammary glands and other sexual characteristics of the female.

The earlier view of Pflüger that the functional correlation between ovary and uterus was through the nervous mechanism, is no longer tenable (34). Neither is the occurrence of menstruation connected with the ripening of the Graafian follicle, for Heape has shown that in monkeys menstruation may occur in the absence of either ripe Graafian follicles or *corpora lutea* (32). It has also been noted that in bats copulation occurs in the autumn, and ovulation is not observed until the following spring, the spermatozoa being stored in the uterus during the period of hibernation. It can thus be seen that the Graafian follicle can have little to do with estrum. Fraenkel (35) has stated that menstruation is brought about by the effect of an internal secretion elaborated by the discharged follicle or *corpus luteum*. He also regards the *corpus luteum* as the only ovarian organ of internal secretion and as being responsible for the estrus cycle as well as the raised nutrition of the uterus during pregnancy. Fraenkel regards the fact of its recurrence following the menstrual period in women, and its monthly regeneration as proof of the importance of the *corpus luteum* as an organ of internal secretion. This, like the above theory, is held by Marshall (34) to be untenable, because it will not account for the sexual phenomena in the lower animals. Most animals ovulate when proestrum is over, so that the *corpus luteum* is usually not present when estrum or "heat" begins. Further proof exists in the female rabbit and cat where ovulation occurs only after copulation, and in the absence of the male, *corpora lutea* are not formed in the ovaries, yet these animals show periodic heat periods.

To summarize all these facts it seems, as Marshall states, the proof of "heat" can not lie in the internal secretion elaborated by the *corpus luteum,* but the theory does seem to explain the raised nutrition of the uterus during gestation, and also is a determining factor in the development of the mammary glands and in the continued existence of the fetus in the uterus at least during the early period of pregnancy. Marshall (34) has shown that "heat" is not dependent upon the development of the Graafian follicle nor upon the *corpus luteum* and suggests that its occurrence must be accounted for by the secretion from the interstitial cells, altho no proof can be adduced showing cyclic changes in these cells. Marshall states further that, "The ovary is an organ providing an internal secretion which is elaborated by the follicular epithelial cells or by the interstitial cells of the stroma. This secretion circulating in the blood induces menstruation and heat. After ovulation, which takes place during estrum, the *corpus luteum* is formed, and this organ provides a further secretion whose function

is essential for the changes taking place during the attachment and development of the embryo in the first stages of pregnancy." It is probable also that it is intimately concerned, through its internal secretion, with the development of the mammary glands, and that the hormone elaborated by the ovarian stroma has to do with the maintenance of the general metabolic equilibrium, and the development of female secondary sexual characteristics. The rôle of the ovary in influencing the general metabolic state has long been known. It has an intimate relation with other glands of internal secretion, changes in one of which seem to derange the others. The possibility exists that this latter function resides in the *corpus luteum,* but definite evidence of its function in the ovary is still unknown.

That *corpora lutea* do not play an important rôle in the estrus cycle is shown, too, by the fact that they are not present during proestrum, and as ovulation occurs in either late proestrum or estrum, they can be functional only subsequent to their appearance, that is, after ovulation. Fraenkel maintains that the *corpus luteum* of the previous ovulation induces estrum of the succeeding one, but as a matter of fact, the previous *corpus luteum* has generally degenerated into the albicans before the succeeding ovulation appears. Further proof lies in finding that in certain animals estrum and ovulation do not necessarily occur simultaneously. It is a well-known fact that in cows *corpora lutea* retained pathologically cause cessation of estrum and of ovulation, and that the removal of the *corpus luteum* by manipulation per rectum, will within from 3 to 7 days cause the appearance of heat, and the animal may conceive if bred at this time (36). It seems, therefore, that this is additional proof of Marshall's theory that the ovarian secretion having control of estrum and ovulation must be sought for in other portions of the ovarian tissue. The lutein tissue, it would seem, inhibits ovulation, which may be another function of that body during pregnancy when both ovulation and heat are inhibited. Pearl and Surface (37) have shown that extracts of *corpus luteum* when injected into laying hens inhibit ovulation, a further support of the inhibitory action theory of the lutein secretion. Inhibition may be the result of mechanical blocking, but more likely the active secretion of the *corpus luteum* inhibits the ovarian function (or the ovarian secretion) controlling estrum and ovulation, for, as previously stated, its removal when pathologically retained causes estrum to appear. It is also possible that its secretion, if controlling estrum as Fraenkel states, is only elaborated in the period of its regression, a fact which would correspond to the cyclic changes that actually appear. The lutein secretion being most abundant during the latter stages of the regression of the *corpus luteum,* would correspond to

the phenomenon of menstruation, which in itself might be responsible for the phenomenon of heat appearing after the proestral or menstrual state. The climax reached, the uterus undergoes a period of rest and repair. During this period a new *corpus luteum* is formed from the ruptured follicle and as it regresses begins to secrete. Thus the cycle recommences. This is hypothetical and probably not what actually occurs, for Marshall points out that heat appears regularly in rabbits in the absence of the lutein cells.

The entire consideration must be only theoretical until the active principles of the internal secretions of the ovaries and *corpora lutea* can be isolated chemically and definitely separated. The fact remains, however, which is the important thing, that the ovary has internal secretions intimately connected with developmental and sexual changes.

CLASSIFICATION OF STERILITY

No thoroly workable classification of sterility of animals, from a pathological viewpoint, exists. From the clinical standpoint an animal is sterile when she no longer produces young, but the causes are so diversified and prognoses likewise so variable that a fundamental classification is difficult when based upon etiology and pathology. Many authors regard sterility as a symptom of disease, or when no demonstrable reason can be adduced for the condition, as an entity in itself.

The basis for the first subdivision is sex: (1) due to the male, (2) due to the female. This report is confined exclusively to the latter. A further subdivision of either (1) or (2) might be adopted as follows: (a) Congenital (usually absolute), and resulting from absence or arrested development of certain organs of reproduction. Congenital displacement, altho rare, may also be a contributing factor. (b) Acquired (relative or absolute), and the result of (1) acquired displacements or injuries, (2) tumors or cysts, (3) specific inflammations, (4) non-specific inflammatory reactions.

GENERAL CONSIDERATION OF STERILITY

Sterility may be said to result, as a rule, when there are deviations from the normal in the genitalia. Factors which are considered essential to conception are: (1) a normal ovum; (2) healthy and active spermatozoa; (3) normal tubal, uterine, and vaginal secretions and structures; (4) a healthy endometrium in which the fertilized ovum may lodge and develop. Inability to produce young is normal before puberty and in aged cows, also occasionally in healthy lactating animals. Gebauer (38) suggests that cows be regarded as sterile (1) when they have passed their second year without showing signs of estrum; (2) in

stables where sterility is prevalent when cows show no signs of estrum for a period of 8 weeks; (3) when after calving estrum has not appeared within two months.

CONGENITAL DEFECTS OF ORGANS OF REPRODUCTION

Complete absence of the ovaries is rarely met with, while arrested development, altho not common, is more frequently seen. In bovine twins, sexual development is often arrested (90 per cent of cases according to Williams (26) when the twins are of opposite sex. These heifers, for the incomplete development almost always occurs in the female, are known as freemartins. Such individuals are absolutely sterile, unless the defect is a minor one. As a rule the arrest in development leaves the animal without uterus or with one only partially formed, or without a normally developed vagina. These animals are unquestionably sterile. In other cases where only minor defects of the uterine tubes, uterus, or ovaries exist, conception may occur. This arrest in development is sometimes seen in heifers not of twins. We have studied two cases in this work in which arrest in the development of uterus and vagina existed. There were in place of the uterus only partially developed horns and fibrous cords, the remains of the Müllerian ducts. These will be described in detail later. Thus we may have complete absence of any essential organ of reproduction or arrested development. Whether the animal will be sterile or not depends upon the extent of involvement.

DISEASES OF THE OVARIES

A. ACTIVE and PASSIVE HYPEREMIAS and ANEMIAS may occur but are not important from the standpoint of sterility. Active hyperemia occurs in estrum and in infections, the passive type when a general passive hyperemia exists (or locally when venous blood flow is in any way obstructed or retarded). Anemias exist in a general anemic state, and because of obstruction of arterial flow.

B. CYSTIC CHANGES are among the most frequently encountered diseases of the ovaries. Zangger (39), in 1859, seems to have been the first to study this condition. Since then, Hess, Albrechtsen, and Williams have contributed to our knowledge of the condition in cattle.

Ovarian cysts may be divided pathologically as follows:

1. Simple ovarian cysts (retention cysts)
   a. Originating from the Graafian follicle.
   b. Originating from the *corpus luteum*.
   c. Originating from the remains of the Wolffian ducts.
2. Pseudomucinous cystadenomata.
3. Serous cystadenomata.

Pathologists are not agreed on a pathological classification of ovarian cysts. Some hold that they all have a common origin from tubular ingrowths of epithelium. Most workers favor a division into: (a) Retention cysts, (b) cystic neoplasms. Retention cysts may be of three types: (1) Failure of the Graafian follicle to develop normally or failure to rupture with subsequent failure of the *corpus luteum* to form. Thus the follicle becomes distended as a follicular cyst. (2) Cystic degeneration of the *corpus luteum,* at any time during its development, but usually when pathologically retained. (3) Another type of retention cyst is seen especially at the hilum or on the broad ligament. These form from cystic remains of the Wolffian duct and attain a great size. This type is infrequent in cows.

Superficial follicular cysts can not be distinguished grossly from normal follicles except that they are larger than the ripe follicle, but size alone is no criterion. Often they are small and multiple. Again they may be large and single. Frequently too, ovaries containing one large cyst and two or three smaller ones are noted. These cysts vary in diameter from microscopical size to 18 to 25 mm. (or more), the average being between these extremes. They are thin-walled when occurring superficially, but the walls are thicker when in the deeper ovarian structures. The epithelium, which is always in part retained in the follicular cysts, becomes stretched and flattened and lies on its basement membrane. The cavity contains a straw-colored serous fluid, usually thin but often mucinous with or without the presence of the ovum (usually without). Sometimes the Graafian follicle only partially develops and then begins to degenerate. The *stratum granulosum* may be partly destroyed. The cavity is always distended with fluid, which microscopically appears as a dense homogeneous eosin-staining mass. Such cysts may be small and multiple or may enlarge to great size. These will be described in detail in the case reports.

Corpus luteum cysts are similar in appearance, except that in place of follicular epithelium around the inner wall, lutein cells and connective tissue are always found. The fluid is often darker in color and may even be blood stained. It is usually thin, but in one of our cases it was of a thick, gelatinous consistency and yellow in color.

Embryonal remains of the Wolffian ducts are occasionally cystic but are very infrequent in cattle. They are most often found on the broad ligament.

The cystadenomata are not often described in veterinary literature and are therefore of little importance in sterility. Kitt (40) reports them as developing to the size of 20 to 30 or even 90 kilos in weight in the mare and cow. They are true neoplasms arising from continued ingrowths of either Pflügers egg cords or superficial ovarian germinal

epithelium. This ingrowth ordinarily is not continued after birth, but when it occurs it gives rise to these adenomatous structures. Cavities lined with simple cuboidal epithelium supported by a connective tissue stroma is the characteristic picture presented. The growth of epithelium spreads from the parent cyst. Daughter cysts are thus produced until a multilocular arrangement is formed. The epithelium secretes either a serous fluid or a pseudomucinous one, quite jellylike in consistency. Either simple or papillary arrangement of the epithelial lining may be the typical appearance. When completely removed the cystadenomata do not recur, neither do they metastasize, but grow from the original focus, along the abdominal peritoneum until eventually they may approximate the border of the liver. In some instances they give rise to carcinomata. It is probable that cysts may also be formed from the structures just described without exhibiting any marked neoplastic characteristics, but there is always a potential growth impulse in their make-up.

The etiology of retention cysts is not known. Rosenau and Davis (41) have associated *Streptococcus viridans* with cystic disease of the ovaries of women. Fitch (42) in his studies found streptococci and *B. coli* in cystic ovaries. Loeb (43) has been able to produce cysts by underfeeding guinea pigs. Only by excessive underfeeding was he able to produce the condition, and then with considerable regularity. Ewing (58) states that the "Fairly constant occurrence of inflammation of the pelvic organs points to the inflammatory origin of these cysts." It is possible that abnormal conditions or infections of the uterus exert a reflex influence upon ovarian function with, possibly, cysts as one of the ovarian changes produced. In regard to etiology of cystadenomata we know nothing more than that they are neoplasms, arising probably as has been suggested.

The symptoms produced by cystic ovaries are usually those of nymphomania. Frequent and irregular heat periods, usually with inability to conceive are often observed, because of abnormal ova or absence of ovulation: Absence or suppression of estrum is sometimes seen as a sequel to cystic ovaries.

C. PATHOLOGICAL RETENTION OF THE CORPUS LUTEUM is often noted. It has no special pathology, simply a retention and hypertrophy of the "yellow body," which for some unknown reason fails to degenerate into the *corpus albicans*. Its retention frequently results in suppression of ovulation and estrum. If estrum occurs, copulation is seldom followed by conception. Usually after some months, the *corpus luteum* becomes encapsulated within a firm connective tissue wall. The lining cells are connective tissue, within which are lutein cells, the remains of the *corpus luteum*. The etiology is unknown.

D. Sterility may result from a general DERANGED METABOLIC STATE through the influence it may have upon the ovary. Glands of internal secretion have been demonstrated as playing an important part in the physiological development of the female, and in general body health. Overwork, insufficient food, high protein diet, obesity, and emaciation all render the ovary less responsive and sometimes result in temporary sterility or weakened and irregular estrum.

E. OÖPHORITIS.—Inflammations of the ovary are acute or chronic. The acute types are most often associated with abscess formation from extension of peritonitis, perimetritis, or salpingitis. The chronic types produce proliferative changes with resulting scars and adhesions. The causes may be tuberculosis, actinomycosis, or pyogenic infections produced by streptococci, staphylococci, or *Bacillus pyogenes*. The infection usually enters the ovary following rupture of a Graafian follicle. Sterility produced thereby is almost always absolute.

F. TUMORS:—Both carcinomata and sarcomata are rarely primary in the ovary, the former being the most common. Dermoid cysts and teratomata are also not infrequently seen, but in cattle are rare. The presence of such growths results in loss of ovarian function with or without symptoms of nymphomania, and in sterility. The cystadenomata have been previously described.

G. SENILE ATROPHY OF THE OVARY is normal in old animals. The rupture of each follicle leads to the development of a *corpus albicans*. This is simply a scar which remains as a result of degeneration and fibrous replacement of the *corpus luteum*. With increasing years these gradually accumulate and undergo hyaline degeneration so that in ovaries of old cows the surface will be seen studded with scars, the *corpora albicantia*. Primitive ova become exhausted or cease to develop into mature follicles. This we speak of as senile atrophy, and representing as it does loss of ovarian function, produces sterility. The period in the animal's life at which this change occurs is not definitely set as in the human, for so far as is known animals do not pass through the menopause. Sometimes the early development of senile changes results in sterility from atrophy in young animals.

H. It is not infrequent to see sterility in cows, with suppressed or feeble estrum, irregular periods, or even complete absence of estrum, when on careful necropsy NO EVIDENCE OF DISEASE, either gross or microscopic, can be found in any organ. Some of these, it is suggested, result from derangement of the endocrines. others are possibly the result of reversion upon the part of the animal to the wild state where estrum in the "Ungulata" occurs but once a year. Suppressed estrum may be an expression of the long anestrous period common to the species before domestication. Marshall (33) cites the observation

that wild monoestrous animals belonging to the same order in the kingdom as the bovine species, when placed in captivity change to polyestrous types, through change in habit. If this is true, reversion in the other direction, influenced by physical factors, is also possible and may explain long continued absence of estrum in some animals when no other cause can be adduced.

DISEASES AND AFFECTIONS OF THE UTERINE TUBES

The importance of diseases and defects of the uterine tubes in relation to sterility can not be overestimated. It must be kept in mind that the uterine tubes are the ducts of the ovaries and the ova must pass through them in order to reach the uterus. It will be remembered that their lumen is narrow, their structure delicate, and their mucosa thrown into folds, directed toward the center, so that injuries, altho slight, may result in temporary or permanent sterility. One normal tube is all that is necessary for conception but, as a rule, infections are bilateral, thus rendering both sides impassable to ova. It is said that simply the loss of cilia from the epithelium is sufficient pathologic change to produce sterility.

A. SENILE CHANGES, or atrophy of the tubes, are normal in aged animals (in women after the menopause). The chief characteristic of the change is atrophy, the tubes becoming smaller. Atrophy frequently results from pelvic adhesions, brought about by infections and pelvic tumors. It may also result from impaired circulation secondary to ovarian cysts, or degenerative changes in the intima of arteries and arterioles supplying the tubes.

B. CIRCULATORY DISTURBANCES are:

1. Anemias, from local obstruction or a general anemic state.
2. Hyperemias
   (a) Active, during estrum and resulting from infection.
   (b) Passive, occurring as a result of obstruction to return flow of blood, general congestion, thrombosis of the ovarian veins or tumors pressing upon them.

In active hyperemias due to infections we have the only circulatory disturbance of any importance in sterility. The typical picture of inflammation is produced. In passive hyperemias the tubes appear blue, the typical picture of retarded outflow of blood.

C. HEMATOSALPINX, the accumulation of blood in the uterine tubes, occurs as a result of tubal pregnancy, or twisting of the tube resulting in passive congestion and tubal hemorrhage. Such twists may be produced by ovarian tumors and ovarian cysts. It may result in rupture of the tube with fatal hemorrhage, or the clot may undergo organization,

thus destroying the function of the tube through stenosis. Tubal pregnancy is rarely seen in the bovine species.

D. ACQUIRED DISPLACEMENTS may be seen, as torsion or adhesions of the tubes. These frequently follow torsion of the uterus, ovarian tumors or cysts, adhesions brought about by parauterine infections or other inflammatory reactions, such as are produced by peritoneal tuberculosis. Adhesions may occur without torsion and occlude the duct, thus rendering the lumen impassable to ova. In these, most often bacterial infections are the cause, and the changes seen are for the most part similar to those described for chronic salpingitis. Many times as a result of ovarian cysts the tube undergoes torsion near the ampulla. This results in occlusion of the duct, and the tubal and ovarian secretions (from ruptured cysts) are dammed up behind the stenotic portion. Thus by close adhesion to the ovary, tubo-ovarian cysts are formed. The importance of displacements of the uterine tubes to sterility, lies for the most part in the possibility of bilateral involvement.

E. INFLAMMATIONS OF THE UTERINE TUBE are known as salpingitis. When involving the mucosa, they are designated endosalpingitis; the mucosa and muscularis, simply as salpingitis; and when involving the serosa, perisalpingitis. It is rare that the mucosa alone is attacked, probably only in the early stages of inflammation is it seen independent of deeper involvement. Perisalpingitis may occur from within outward, or by extension from the abdominal osteum of the tube. Very frequently it follows parametritis and perimetritis, with resulting adhesions and displacements as already described. Extension of tuberculosis may also be a cause. Salpingitis is by far the most frequent and most important condition seen in the uterine tubes. It may be divided into acute and chronic catarrhal salpingitis, and acute, subacute, and chronic purulent salpingitis.

Etiology. In the bovine species, as in woman, it may be said that salpingitis occurs only as the result of bacterial infection, the most common invaders in cattle being *Bacillus pyogenes* (Lucet) and streptococci, with staphylococci usually present but playing a secondary rôle. Salpingitis very seldom occurs acutely, except as a result of puerperal infection, but may occur (as in one of our cases) by extension of pyometra in a virgin heifer. The relation of *B. abortus* to salpingitis is merely as a predisposing factor, preparing the way for pyogenic infection of the uterus, with a secondary salpingitis. It may rarely result from the extension of peritonitis or pelvic abscesses. Theoretically, salpingitis may be primary and of hematogenous origin, but practically this never occurs. Salpingitis is often bilateral.

The results of salpingitis are (1) permanent damage, and (2) no permanent damage to the tube. Its extension to the peritoneum often causes peritonitis, either localized in the pelvic region with formation of large abscesses or generalized. Fusion with the ovary not infrequently results in the formation of large tubo-ovarian abscesses. Then, too, it may heal in the incipient stage and complete recovery result.

1. Catarrhal salpingitis occurs acutely as a preliminary stage in the course of inflammation of any mucous membrane and is most of the time not the stage of inflammation resulting in serious damage. It is a transitory outpouring of mucus seen in the congestive stages of inflammation. Gillman (44) has described chronic catarrhal salpingitis as producing productive inflammatory changes in the tubes with resulting stenosis and hydrosalpinx. Organisms may be of sufficiently low virulence to produce such changes, but it seems more likely that most of the chronic changes result from old purulent infections. In catarrhal salpingitis lymphocytes are the predominating cells in the inflammatory exudate, rather than polymorphonuclear leukocytes. The process and changes are similar to those described for chronic purulent salpingitis. It is a low-grade chronic type of inflammation from the start.

2. Purulent salpingitis may be conveniently divided into acute, subacute and chronic. The subacute stage is an arbitrary division to indicate the gradual progression into the chronic type.

The acute form is ushered in by the ordinary inflammatory reactions, congestion, edema, and exudation. As is true of inflammatory reactions on all mucous surfaces, the first change seen is congestion, during which time there is a serous or catarrhal exudate. In case the infection is halted here, no further change occurs, and the mucosa goes on to repair. Either healing results or the process proceeds to the next stage. The increased secretion (or catarrhal stage) is followed by exudation of polymorphonuclear leukocytes, red blood cells, lymphocytes, and plasma cells. At first few in number, they gradually increase until the exudate appears muco-purulent. The clear mucus is streaked with pus. Gradually it becomes more purulent and contains the cells and debris ordinarily seen in any purulent exudate. The tube is swollen, and distended with pus which has free drainage to the uterus. In the beginning the walls are stretched and thin, but if the process continues they become thick through organization and proliferation of highly vascular connective tissue. This results in a tortuous or kinked tube. Microscopically the lumen of the tube is seen to contain a purulent exudate, consisting of inspissated serum, fibrin, polymorphonuclear leukocytes, a few lymphocytes and plasma cells, bacteria, and detritus. The epithelium is irregularly degenerated, owing to the action of the bacteria, but always shows less involvement than would be expected.

The crypts between the mucous folds form pus pockets. Microscopic abscesses may be seen in the mucosa and *tunica propria*, even extending to the muscularis coat. If healing is to occur and leave an unimpaired tube it must take place at about this stage. If healing does not result the whole process gradually passes on through subacute and chronic stages from which recovery of function is impossible.

The chronic stage, the one almost always seen at necropsy, is dependent upon the continued progress of the infection. Bacteria invade the deeper structures of the tube, producing greater kinking and greater thickening of the walls. Marked changes appear in the mucosa. The epithelial folds, ordinarily quite delicate, become greatly hypertrophied and often adhere to one another. Later actual growth from one to another and across the lumen occurs, and with the gradual distention of the tube they continue to grow, appearing as thin-walled, small, multilocular cavities. The epithelium is yet, for the most part, intact. The exudate gradually subsides and in place of polymorphonuclear leukocytes as seen in the acute stage, the predominating cells seen in the exudate are lymphocytes and plasma cells, with much fibrin. Organization or lysis of the exudate usually begins at this stage. In case of the former the process may progress slowly with gradual diminution of the exudate and progressive organization. The walls become permanently thicker, the mucosa may entirely disappear or the mucous folds, through fibrosis, may become obliterated and thus contribute to the thickening of the wall. Many times this leaves the base of the folds below a solid fibrosed area, as remnants of tubal epithelium. In cross-section these remnants appear as acini of glands. This process may continue to complete stenosis of the duct, with disappearance of the exudate. It often happens that the rate of proliferation and organization is more rapid at one point than another, probably aided by kinking of the tube with stenosis. The favored site for early stenosis is the abdominal osteum with later stenosis at a point below the ampulla. As a result of this stenosis the exudate collects and distends the tube. The adherent mucosa remnants become stretched but are usually sufficiently strong to retain their attachments. The dammed-off portion of the tube in this state of pus distention is known as pyosalpinx (pus tube). It seems that in cattle the distention in salpingitis is never so great as in woman, for rarely are the adherent mucous folds pulled apart or separated and flattened out, but retain the multilocular character. The microörganisms gradually die or are already dead at this time. The pus is gradually absorbed and is replaced by a clear, watery, light straw-colored transudate, or later by mucous secretion from the regenerated tubular epithelium. The fluid contains but few leukocytes. Bacteria may be found present

from the active inflammatory process which preceded, but if careful cultural methods are employed the fluid will usually be found sterile. This last type or stage we designate hydrosalpinx. We are not sure that salpingitis always proceeds as here pictured, but the changes seen indicate previous active infection, for all transitions can be noted between the infective stage and the final. The typical appearance of hydrosalpinx in cattle is a more or less enlarged, thin-walled, tortuous tube, containing a clear fluid. The lumen is marked off by adherent and stretched mucous folds, appearing as small multilocular cysts. Each fold is supported by its basal membrane and lined by quite normal appearing epithelium. It is possible by sufficient distention of the tube to have the flask- or retort-shaped pyosalpinx and hydrosalpinx as seen in women, but we have observed this form only once. One of us has a specimen of this type. Frequently at autopsy only the ampulla will be seen involved. It seems that the uterine end of the tube very often heals but leaves a stenotic ampulla. The ampulla then passes on to chronic salpingitis ending finally in hydrosalpinx and leaving the uterine end of the tube unimpaired. Sometimes the stenosis occurs near the isthmus, in which case the entire tube passes on to chronic salpingitis. The results of salpingitis after the acute stage has passed and the chronic stage begun can always be regarded as producing incurable sterility, in so far as cattle are concerned.

F. Of the SPECIFIC INFECTIONS, tuberculosis and actinomycosis are the only two involving the uterine tubes. Grossly either may appear like a pus tube, or purulent salpingitis, but they are easily differentiated microscopically. Tuberculosis is nearly always secondary to an already existing focus of infection, while actinomycosis is more often primary in the genital organs. In tuberculous salpingitis the tube is swollen and reddened, and pus is found in the lumen. In chronic cases the tubes thicken and become firm and filled with caseous exudate, containing inspissated serum, a few polymorphonuclear leukocytes, plasma cells, and many lymphocytes. Miliary tubercles with or without calcification develop throughout the walls. The reaction involves the mucous folds which become adherent by organization and extension of the tuberculous process and are often entirely replaced by the tubercles and caseation necrosis. In milder cases remnants of epithelium will be seen deep below the newly formed tissue, in this respect appearing often like acini of glands without outlet to the surface. Sometimes in chronic cases the tubes appear beaded through twisting and bulging of the walls, caused by the developing tubercles. The outcome of tuberculous salpingitis may be tuberculous peritonitis, tuberculous metritis, extension to the ovary, generalized miliary infection from invasion of the blood stream, pyosalpinx (pus tube), or a chronic tuberculous salpingitis with-

out healing, but usually with occlusion of the tube. As tuberculosis is usually bilateral, permanent sterility is in most cases an inevitable outcome. Actinomycosis, when developing in the uterine tubes, causes extensive pelvic involvement through extension, by the development of fistulae. It is similar in appearance to actinomycosis elsewhere, and invariably results in permanent sterility of fatal termination.

G. TUBAL GESTATION has been reported in the cow but is so very rarely seen that only passing mention need be made.

DISEASES AND AFFECTIONS OF THE UTERUS

The uterus, of all the genital organs, is the essential one for the development of the embryo. It is often the seat of changes or infections which render the animal temporarily or permanently sterile. The congenital anomalies have been previously mentioned.

A. ACQUIRED ANOMALIES and DEFORMITIES are not commonly seen. They may develop from pelvic and intestinal adhesions following infection, or as the result of tumors of the genital tract or broad ligaments. Torsion of the uterus quite frequently occurs, the cause of which, theoretically, may be similar to those listed for the uterine tubes, but it almost always accompanies gestation. Rupture of the ligamentous attachments of the uterus may render the cow unfit for further pregnancies. Prolapse of the uterus may follow such an accident, but usually results only from dystocia where severe straining and traction are the exciting cause. Lacerations and perforations occur and are usually accidental from obstetrical or surgical manipulation. If peritonitis does not result, these are not ordinarily serious. Loss of cotyledons (carunculae) occurs usually following manual removal of the placenta or following prolapse, but does not as a rule render the animal permanently sterile. It seems rarely to occur.

B. CIRCULATORY DISTURBANCES, such as anemias and hyperemias (acute and passive), are seen. Active hyperemia is physiological in estrum and gestation, and occurs pathologically in inflammations. Passive hyperemias develop as in the uterine tubes. Neither in itself is an important contributory factor to sterility. Anemias may occur as described for the uterine tubes.

C. INFLAMMATIONS are spoken of as metritis, and may conform to the following arbitrary classification, based upon clinical and pathological findings.

1. Acute metritis—mild or severe
   (a) Puerperal infection
   (b) Non-puerperal infection
2. Chronic metritis
   (a) Begins as a low-grade infection and continues as such.
   (b) Develops from acute (a or b) by long continued infection.

Some workers further subdivide into acute and chronic endometritis, myometritis, perimetritis, and parametritis. These terms refer simply to location of the inflammatory process, but from the pathological viewpoint can hardly be said to exist as independent disease processes. One type blends closely with the other, so intimate are the anatomical relations. The term metritis will be used in the broad sense with the other terms as descriptive of location.

Etiology.—Metritis in every instance develops as a result of infection. The predisposing causes may be injury, through trauma or irritating fluids, but these only make possible the invasion by bacteria. Eggink (45), in an analysis of 20 cases of acute and chronic metritis, found the following organisms:

B. tuberculosis	2X	Staphylococci	5X
B. pyogenes bovis	14X	*B. proteus*	3X
Streptococci	12X	*B. subtilis*	1X
B. coli	6X		

In many of these, mixed infections were present. From analysis of cases the most important organisms appear to be *B. pyogenes,* and streptococci. Except in one case of tuberculous metritis, either or both of these organisms were always found. Lucet (46) first described *B. pyogenes bovis* (1893) when he studied 52 cases of suppuration in cattle. In these he found *B. pyogenes bovis* pure in 10 cases and associated with other bacteria in 7 cases. His type has since been found identical with *B. pyogenes suis* (Grips) and the name *B. pyogenes* has been proposed for both. Künnemann (47) studied many cases of suppuration in cattle and concluded that *B. pyogenes* is the most important etiologic agent. He observed this organism in 90 per cent of cases, in 35 per cent pure and in 55 per cent associated with other organisms. In a survey of 18 cases (purulent, acute, and chronic metritis) reported by Wall (16), the following organisms were found:

B. pyogenes	6X
Streptococci	4X
Streptococci and *B. pyogenes*	5X
Streptococci and *B. coli*	1X
Streptococci, *B. pyogenes,* and *B. coli*	1X
Streptococci and an anaerobic bacillus	1X

Ward (64) was the first in this country to report on the importance of *Bacillus pyogenes* in animals. Brown and Orcutt (1920) (48) in their "Study of *B. pyogenes,*" worked with 12 strains of the organism, 5 of which were isolated from cases of purulent metritis. The results of the present investigation, which will appear in detail later, confirm the importance of *B. pyogenes* in bovine metritis.

1. Acute metritis of the mild type generally involves the endometrium alone and thus in mild cases acute catarrhal endometritis is frequently seen. It is nearly always the result of an infectious abortion. It may follow retention of afterbirth of full-term gestation, but more often the latter type is more severe. Following the infection of the uterus and placenta by *B. abortus,* an inflammation is set up which results in the premature delivery of the fetus. This organism is not capable of establishing itself in the normal involuted uterus and soon disappears after the abortion. If no secondary infection follows, only a mild acute catarrhal endometritis will ensue, marked by excessive discharge, muco, and muco-purulent, which as involution takes place will rapidly disappear without permanent changes remaining. The superficial lesions seen in the mucous membrane are necrosis and exudative inflammation. The former is a normal accompaniment of involution in the physiologic discharge of the fetal and maternal placenta. Healing in most cases is complete, but Wall (16) states that shrinkage and atrophy of the gland mucosa may occur, with probably similar changes in the carunculae. This change results in no permanent damage to the organ.

2. Acute metritis of the severe type is in the vast majority of cases puerperal in origin (involving endometrium and often other uterine coats). Death and maceration of the fetus *in utero* is frequently a contributing cause, or it follows either infectious abortion or full-time parturition. In either case retained fetal membranes favor the infection, or it may be introduced from the exterior by the operator or accidentally from the vagina. In the majority of non-puerperal infections it follows injury, often during breeding, or through extension of cervical and vaginal infections. The effect of the abortion bacillus on the uterus, in case there is no retention of the placenta, is simply to cause a mild catarrhal endometritis. If the placenta is retained, and this applies to all forms of retention, the involution of the uterus is delayed. Organisms, both parasitic and putrefactive types, enter through the vagina. The mucosa is not able to resist their entrance and severe purulent metritis develops. The mucosa, following delivery, it will be remembered, is deprived for the most part of its epithelium. Carunculae slough off in part, in order to release the fetal chorionic villi. Other cases develop following dystocia, especially when operative procedure is not properly applied, or simply as accidental infections when the utmost care is exercised. The organisms most often associated with this type of infection are streptococci and *Bacillus pyogenes.* Wall (16) makes the observation that if the infection be due purely to streptococci the process heals quite rapidly, but when

resulting from *B. pyogenes,* either pure or associated with other bacteria, pyometra is the rule. The work presented in this paper supports this view.

Pathologic changes.—The endometrium shows necrosis of varying degrees (partly physiological following parturition). It is usually diffuse. Congestion and edema develop coincident with exudative phenomena. At this time large quantities of mucus lie in the cavity of the uterus. Polymorphonuclear leukocytes are seen in great numbers and form a considerable portion of the exudate. The leukocytes gradually increase in numbers until the exudate is decidedly purulent, appearing as thick, creamy pus. As a result of the action of putrefactive bacteria, decomposition of the pus sometimes is noted. *Bacillus proteus,* anaerobic bacilli, and other proteolytic soil types are responsible for the offensive odor. This has nothing to do with the progress of the infection. In the mucosa may be seen large numbers of polymorphonuclear leukocytes, lymphocytes, eosinophiles, and plasma cells, often collected in groups to form microscopic abscesses (not to be mistaken for the normal lymphoid tissue of the uterus which is also accentuated as a result of disease). These even may extend to the muscularis and serosa, but not as a rule. The gland epithelium becomes necrotic and in many cases lost; other glands are blocked in their course by proliferative changes and appear as small cysts. The epithelium of the mucosa generally regenerates but is not of a healthy type, neither is it entirely regenerated during the course of the infection. It is surprising in studying cases of purulent metritis to see the uterus as healthy as it invariably is. The changes in the wall are in no way commensurate with the exudate in the lumen. This type heals early or passes on to the subacute and chronic types.

Symptoms produced are those of general sepsis, as anorexia, slight fever, stupor, and cachexia. As a rule, these symptoms are not marked unless retroperitoneal abscesses develop (localized peritonitis).

Acute metritis may continue to chronic metritis, with development of salpingitis, perimetritis, abscesses of the parametrium (localized peritonitis), ovarian abscesses, or generalized peritonitis with fatal termination. Thrombosis of veins in the vaginal plexus may occur. In other cases it may continue to pyometra as a subacute inflammation, uncomplicated for several weeks, and result in complete recovery when properly treated. Then, too, the condition may have a favorable termination in the incipient stage (especially when of the streptococcus type).

3. Chronic metritis.—In most cases after an acute attack the purulent discharge seems to subside and the observer will think the case healed. This is an expression of closure of the cervical canal. In

many cases, the uterus fails to undergo involution following parturition (subinvolution of the uterus) and throughout the acute attack remains in the evolutionary stage. It gradually fills with the purulent exudate already described, until possibly 5 liters collect. It then begins to ooze from the vagina when the animal is decumbent. This damming up of the exudate we speak of as pyometra. There appears to be in cases of infected uteri, together with the failure of the uterus to undergo involution, also the failure of the *corpus luteum* to disappear (persistent *corpus luteum*), exemplifying the close physiologic relationship existing between the two organs—ovary and uterus. In other cases free drainage is continuous with apparently the same uterine changes, simply a purulent metritis. The course is similar to that already described in acute metritis, and the complications there described are more often delayed until the chronic stages. Recovery in simple purulent metritis without complications, under proper treatment, is often noted. Pathologic changes are similar to those already described for acute metritis, simply more pronounced. The proliferative changes are accentuated, as are also the changes in the gland mucosa. Wall (16) describes regeneration of the normal uterine epithelium by ectodermal types of epithelium as seen in the vagina. This he calls "ectodermoisering." He regards this as a permanent change, affecting the usefulness of the organ. The fibrous tissue is accentuated by proliferative changes, and in the muscularis Wall (16) observed atrophic changes, at other times hypertrophy, depending upon the type of infection. Fibrosis may be so severe that the uterus becomes very hard and thick. In this state the organ is called sclerotic. We have studied and one of us has treated several cases of chronic metritis with excellent results, complete recoveries having occurred.

It is possible that even tho no palpable lesions exist there are physiologic disturbances, producing altered secretion of the glands. The normal uterine secretions, in order to support fertilization of the ova, must be neutral or faintly alkaline. Spermatozoa are killed in acid secretions. Such abnormal secretions are well-known in women and probably give rise to many cases of sterility. If such changes occur in the uterus of the cow no doubt they exert a similar action on the spermatozoa. Since there is a successful treatment for such conditions (alkaline douches) an investigation of this should be continued when material is available.

Hallman (59), in a report on the pathologic findings in eleven cases of bovine sterility, observed alterations of the uterine mucosa varying from slight fibrous thickening of the transverse cervical folds with no apparent alterations of the corporal and cornual mucosa to an atrophic

endometritis. "The lesions observed in varying degrees in the different cases are mucoid degeneration of the superficial epithelium, local and diffuse fibrosis of the uterine mucosae, leukocytic infiltration of the stroma and gland luminae, and degeneration and disintegration of the glandular epithelium with dimunition in the number of glands. In the majority of cases the anatomical alterations are comparatively few and it is hardly conceivable that failure to breed was the result of loss of functional tissue of the uterine mucosa." The studies in the investigation here reported support this view.

4. Chronic catarrhal endometritis is a clinical subdivision of ordinary chronic metritis and the term is used to designate a chronic catarrhal metritis in which there is little formation of purulent exudate. The infection begins usually following abortion or full-term parturition and continues as a low-grade inflammatory process, causing increased secretion and hypertrophy of the mucosa. Cystic and large tortuous glands are often seen. At other times they are atrophic. There is frequently a mucoid degeneration of the mucus secreting glands. From reliable sources the information has been obtained that 90 per cent of the curettements from women, in which curettage has been done for chronic catarrhal endometritis, are normal and that the symptoms observed are the result of altered ovarian function, in most cases, with no evidence of an inflammatory endometrium. It is better to regard these cases, when no active infection can be demonstrated in the endometrium and where pathologic changes exist, not as active inflammations but as the result of acute or chronic metritis, as already described.

D. HYPERTROPHIC ENDOMETRITIS is occasionally seen in the bovine species (60). The uterine mucosa in these cases becomes much thickened. It becomes very vascular and quite susceptible to hemorrhage. The glands enlarge and become cystic and on the surface of the mucosa there develop irregular rounded polypoid-like projections. Many of the cases diagnosed as hypertrophic endometritis, in human practice, have simply been physiological changes of menstruation. There is no doubt, tho, that this type of disease exists. It results in incurable sterility, for in the bovine species curettage is not practiced. The cause is unknown, but by many it is regarded as inflammatory.

E. CYSTIC DEGENERATION OF THE UTERINE WALLS WITH HYDROMETRA is described by Williams (60). It is the outcome of many pyometra cases, all severe cases being more or less affected. The uterine glands become cystic, and the uterus may contain much clear fluid. The mucosa grossly appears studded with cysts. Microscopically large, dilated uterine glands are seen. It results from inflammation, a termination of chronic metritis.

F. SPECIFIC INFLAMMATIONS are produced by *B. tuberculosis* and *Actinomyces bovis* and are essentially the same as infections produced elsewhere by these organisms. Sterility with systematic complications usually results, or else these infections are secondary to some more generalized lesions already existing.

G. HEMATOMETRA, distention of the uterine cavity with blood, is rarely seen in the bovine species. Williams (26) describes these cases and states that not infrequently the clot may undergo organization and result in a large uterine hematoma.

H. TUMORS of the uterus, according to Williams (26), are rare. From comparative pathology, leiomyomata should be the most common, with adenomata and carcinomata second. Chorionic epitheliomata and fleshy placental moles have been observed in the bovine species. Tumors, when present, result in sterility, especially when large or growing rapidly.

DISEASES AND AFFECTIONS OF THE CERVIX

As no special attention has been directed toward the consideration of cervical and vaginal diseases which may lead to sterility, only a brief resumé of these will be given in this report.

A. OCCLUSION OF THE OS UTERI, with a cervical canal so tightly closed that spermatozoa can not enter, is rarely found in cows.

B. DILATION OF THE CERVIX UTERI, through loss of muscular tone, is occasionally seen and often the atony is so great that conception can not occur. It is an accompaniment of atony of the uterus in nearly all cases.

C. HYPERTROPHY OF THE EXTERNAL OS UTERI frequently occurs as a result of low-grade proliferative inflammations following injuries at parturition through use of instruments or from extension of vaginal infections. Grossly the folds show great hyperplasia so as partly to block the cervical canal. The mucosa is hyperemic, and often covered with small red papules and vesicles. The epithelium is usually thickened and edematous, while, as a result of rupture of vesicles, it may be desquamated in some places. Sterility is sometimes an accompaniment, but only temporary, until surgical relief can be applied, unless, as is frequently the case, the hypertrophy is occurring with a severe *B. pyogenes* or streptococcus cervicitis and metritis.

D. INFLAMMATIONS OF THE CERVIX AND EXTERNAL OS UTERI often occur as the result of irritating douches, and unless infection supervenes they are only transitory. Infections frequently follow injury at parturition or from use of surgical instruments. They also may develop from extension of metritis and vaginitis, or may be primary at any time. Such infections usually develop slowly with exudation and

proliferation and probably are in most cases caused by streptococci or *Bacillus pyogenes*. The arrangement of the cervical folds in plaits of the mucosa serves to make the infection an obstinate one and difficult to treat. The most frequent complications are hypertrophy of the cervical folds, adhesions resulting in atresia, and extension of the infective process to the uterus and other genital organs. Increased tenacious secretion may result and lead to sterility through mechanically entangling the spermatozoa before they gain entrance to the uterus. This produces a temporary sterility, and in human practice has been found quite amenable to treatment (saline douches). Sterility is present during the infection, but if the infection subsides before pathologic changes are great, judicious treatment usually effects a cure.

E. TUMORS such as polypi are reported, but these growths are rare. Malignant carcinomata are not reported as occurring in the cervix of the bovine species.

DISEASES AND AFFECTIONS OF THE VAGINA

A. CONGENITAL ABNORMALITIES.—The persistence of the hymen into adult life is occasionally seen and leads to sterility until operative removal. Sometimes a small opening is noted, while in other cases none exists. Bands are sometimes seen representing the embryonic median walls of the fused Müllerian ducts, which have failed to atrophy and disappear completely. They may persist so completely as to constitute essentially a double vagina (Williams (26)). They can, as a rule, be reduced by surgical procedure so that permanent sterility is not a result. The almost complete absence of vagina in freemartins and other anomalies and arrests in development of the genital tract have been mentioned.

B. ACQUIRED ANOMALIES AND DEFECTS.—Between the walls of the vagina, as the result of proliferative changes following infections, strong connective tissue bands frequently develop resulting in atresia of the vaginal walls. One such case is included in the case reports which follow. The stricture, when extensive, renders the animal sterile; when slight, surgical interference usually results in recovery.

C. HYPERTROPHY OF THE VAGINAL WALLS.—This is frequently seen, occurring during the late stages of gestation and in the non-pregnant animal. The wall of the vagina, 10 to 12 cm. anterior to the vulva, laterally and dorsally becomes hyperplastic so that partial prolapse of the vagina results, ordinarily seen only while the animal is decumbent. Severe inflammatory changes sometimes develop and result in more complete prolapse, induced by straining from the irritation. The condition is ordinarily successfully treated through surgical removal of the hyperplastic portion of the wall.

D. PROLAPSE OF THE VAGINA is seen in cases other than from the development of hypertrophic walls. It is occasioned by late pregnancy, especially in fleshy animals, and from injuries following parturition. The prolapse is frequently not complete, and is visible only while the animal is decumbent, but may be severe and complete.

E. VAGINISMUS (violent spasms of the vagina) is a frequent symptom of disease of the genital tract and ovaries. These spasms influence conception and may be relieved when the cause is removed. Their influence on conception in the animal is only secondary.

F. CYSTS OF GÄRTNER'S DUCTS (remnants of the Wolffian duct) may interfere with successful breeding but do not result in absolute sterility.

G. CYSTS OF BARTHOLIN'S DUCT are described by Hess (49) and Hofman (50). The glands and ducts become hyperplastic and cystic. Until surgically removed they may prevent conception.

H. INFLAMMATIONS in most cases are the result of infections. Injuries or irritating chemicals may influence their development. Two types of inflammatory changes are seen:

1. Granular venereal disease.
2. Non-specific purulent inflammations.

1. Granular venereal disease is an infectious vaginal disease, occurring very commonly in cows (according to Williams in 86 per cent of cows examined). It is characterized by the development of hard, yellowish granular nodules on the edematous vaginal mucosa. The etiologic agent has not been definitely determined but most workers favor the streptococcus as the cause. Williams (51) called attention to the prevalence of the condition and its possible relationship to infectious abortion, but *B. abortus* probably has no relation to the condition. Pathologic changes are hyperemia and edema of the vaginal mucosa, with the formation of tiny granular yellowish vesicles. Increased catarrhal exudate is an accompaniment. The vesicles are an enlargement of the lymph follicles, which, owing to the inflammation, are edematous, swollen and hyperemic. The disease probably has no relation to sterility, except that through its presence saprophytic bacteria of the lactic acid type enter and render the secretions acid, thus inhibiting the penetration of living spermatozoa into the uterus. Other saprophytic types may through enzymic action so attenuate or kill the spermatozoa that fertilization of the ova is impossible.

2. Nonspecific purulent inflammations occur principally following parturition. They are of comparatively infrequent occurrence. The majority of cases seen and diagnosed vaginitis clinically, are simply drainage of pus from the uterus and cervix without inflammatory reaction in the vagina. The vagina, because of its stratified epithelial

surface, is not prone to become infected unless already mechanically injured any more than is the external surface of the body. No study has been made of vaginitis but probably *B. coli* and staphylococci are more often the etiologic agents than are streptococci or *B. pyogenes*. The pathologic changes are similar to those seen on any mucous membrane, and are in most cases only acute, accompanied by a mucopurulent discharge.

I. TUMORS, such as polypoid masses and papillomata, are sometimes seen but are not common. Carcinomata and sarcomata are rarely seen in this location, in the bovine species. Williams states that carcinoma of the vulva is not rare in the cow.

J. DISEASES OF THE PELVIC BONES, altho rarely seen, are productive of sterility in that the animal can no longer carry the fetus properly. Fracture of the ileum through injury may be responsible for this condition. Osteomalacia may render the pelvic bones friable and result in narrowing of the pelvic inlet to such an extent that parturition is difficult or impossible. So-called dropping of the tail head (sacrum) may produce a similar result. In nymphomania (cystic ovaries) the tail head often becomes raised through relaxation of the pelvic ligaments. Misplaced genitals may result, but are returned to normal when the cause (cystic ovaries) is removed.

THE PRESENT INVESTIGATION

METHODS OF STUDY

The object in view during the progress of this investigation has been to obtain cases which were diagnosed by clinical procedure as sterile. Sterility in some instances was considered as absolute, and cases falling into this group were slaughtered and the genital organs studied both pathologically and bacteriologically. Clinical history, altho not always complete, is available in all cases of this group. Other animals were presented at the University clinic for treatment of sterility, the majority of which responded favorably to the clinical procedure employed. Improvement in this group was apparent, with suggestion of recovery. Since the affected animals were valuable purebred stock, slaughter was not advised. In these cases bacteriological studies combined with clinical data constitute the report. When possible, cultures were obtained from the genital tract (uterus) during the progress of the infection by inserting sterile swabs through the cervical canal into the uterus. The same method was employed in all cases where the genital tract was cultured during the life of the animal. At necropsy the genital organs were carefully removed, and systematically cultured. The organs were seared at the point of study

and penetrated with sterile instruments. At the point of penetration, material for cultural study was obtained. Cultures were prepared on 10 per cent sterile horse serum agar and the tubes sealed with hot wax. These were allowed to incubate from 10 to 14 days at 37°C. By this method types such as *Bact. abortus* could develop. The aerobic cultures were prepared by the plate method, using agar in combination with sterile defibrinated horse blood. By this method streptococci and *B. pyogenes* were most easily obtained in pure culture. As soon as possible after cultures were prepared, sections were taken from various parts of the genital tract. Preservation and fixation were accomplished in Zenker's solution, and in 10 per cent formalin. Sections were cut by the paraffin method, and also by the freezing method. Hematoxylin and eosin were employed in the staining technique. Cultures were identified individually. In all instances the most modern and also original references were consulted. For *Bacillus pyogenes* the original work of Lucet (46), Künnemann (47), Grips (52), Glage (53), and Brown (48) were consulted. For the work on streptococci, the works of Brown (56) and Hollman (55) have been used exclusively. The work of Winslow (54) et al. has been followed in studies on the staphylococci. In all, nineteen cases are reported, only one without clinical history, this being a case of tuberculous metritis and salpingitis obtained at the abattoir.

CASE REPORTS

CASE I

Clinical history.—Jersey cow, 5 years old. First calf born at two and one half years of age, full term but born dead. Agglutination reaction for infectious abortion, positive up to 1-200, May, 1918. Second calf aborted June, 1918. Received into University experimental herd December, 1918. Bred January 27, 1919; examined and pronounced pregnant March 6; examined again in April, at which time found non-pregnant. It is assumed as reasonably certain that she aborted between first and second examinations for pregnancy. Bred April 14, May 25, and June 24, 1919. The animal never showed any extreme signs of heat, coming in and going out normally. Bred again July 5 and July 29, 1919. Allowed to rest for several months. Uterus examined and massaged without detecting any abnormality. Bred October 18, 1919, November 28, 1919, January 22, 1920, and February 5, 1920. Examined again March 15, 1920, and found to be non-pregnant, genital organs apparently normal. Agglutination reactions of blood to *B. abortus* antigen, after the animal entered the University herd were as follows: November, 1919, and March, 1920, positive 1-20 to 1-1000 and inclusive dilutions. The history of the

animal indicates the prevalence of sterility in the herd from which she came. The mother was difficult to get with calf, but never aborted. After parturition there was usually retention of the placenta. One sister of cow, case 1, was sold for beef because of sterility, and another was recently sent to our experimental herd because of frequent abortions (last three calves aborted). The animal's condition (case 1) was considered incurable, and she was slaughtered March 30, 1920.

Necropsy

1. *Gross description.*—The general condition of the carcass is good. The vagina is normal. The cervix is normal. The uterus appears normal. The *tubae uterinae* appear normal. The right ovary is 3 cm. in length, and 2 cm. in width. It appears to be more adherent than normal to the broad ligament. It contains a *corpus luteum* 8 mm. in diameter. The left ovary is 2.7 mm. long, 1.3 mm. wide. It contains a persistent *corpus luteum* deeply buried in its stroma. The *corpus luteum* is 2.5 cm. in diameter. The center of the *corpus luteum* presents a cystic cavity 1 cm. in diameter. The ovarian tissue is greatly flattened over this retained and cystic *corpus luteum.*

2. *Microscopical description.*—The vagina and *cervix uteri* are normal. In the uterus some of the innermost glands show degenerative changes. The glands are enlarged, and the epithelium of many is partly degenerated. In the lumina there is an exudate containing desquamated cells and mucus. The nuclei of the gland cells are pyknotic. All the deeper lying glands are normal. The stroma of the gland mucosa is less cellular than normal, owing to increased connective tissue proliferation, mostly collagenous fibrils. The other coats of the organ are normal. The uterine tubes are normal. There are many primitive follicles in the cortex of the right ovary. Lying deeper in the ovarian cortex there are three follicles (in one portion of the ovary), showing atretic degeneration. The *theca folliculi* of these follicles is greatly thickened, and is very cellular. The *membrana granulosa* of the smaller follicles is so proliferated as almost completely to fill the central cavity. In the larger ones these cells are increased in number, many of them being detached from their normal attachment and lying free in the central cavity. Many of these cells have pyknotic nuclei and their cytoplasm shows a hyaline granular degeneration. Figure 1 illustrates this condition. *Corpora albicantia* are numerous throughout the ovarian stroma. Several normal, nearly mature, Graafian follicles are present. Other sections appear normal.

3. *Bacteriological findings.*—

1. Cultures from the uterus, uterine tubes, and ovaries remained sterile.

2. Three types of organisms developed from the vagina:

(a) *Staphylococcus aureus* (Rosenbach); (b), *B. coli communis;*

(c) *B. subtilis*

4. *Diagnosis and discussion.*—The etiology of sterility in this case is not clear. Possibly the deep seated cystic *corpus luteum* which was present in the left ovary was a contributing factor. The degenerative changes described in follicles in the right ovary may also have influenced the progress of the condition. The changes in the uterine glands may also have been sufficiently pronounced to inhibit implantation of the developing embryo, or to inhibit passage of spermatozoa to the ovum. The most probable change responsible for sterility is that described for the ovaries.

CASE 2

Clinical history.—Shorthorn heifer. Bred for first time April 3, 1920. Appeared in estrum again April 26, and was rebred to same sire. Immediately after this service the heifer was noticed to be suffering considerable pain. At termination of next diestrum, heat did not appear, but pregnancy was not suspected on account of a fairly copious and constant vaginal discharge. The discharge was of a mucopurulent nature, yellowish gray in color, and had a pronounced offensive odor. The discharge also at times was streaked with blood. A physical examination of the vagina revealed severe tho not active inflammatory changes. The mucous membrane of the vagina was studded with small vesicles, such as characterize granular venereal disease. Cervicitis was pronounced. The *os uteri externum* was covered by a profuse mucopurulent exudate. The cervical canal was partially obstructed by inflammatory changes. A rectal examination was made with considerable difficulty owing to formation of massive adhesions between the uterus, ovaries, and walls of the rectum and colon. This resulted in constriction of the lumen of this portion of the intestinal tract. The right ovary was found to be enlarged and adherent to the right uterine horn. The right uterine tube was sufficiently distended to render it easy to locate and was adherent to the ovary. The left ovary contained a large cyst. It was enlarged and irregular in outline and adherent to the left uterine horn. The left uterine tube was not definitely located. The body and horns of the uterus were difficult to palpate, but were thought to be somewhat hard and thickened. A diagnosis of incurable sterility was made and the animal was slaughtered for food.

Necropsy

1. *Gross description.*—The physical condition of the carcass is good. The vaginal mucosa appears practically normal. The *corpus uteri* is indurated, and adherent by fibrous attachments to the rectum. No macroscopic changes are apparent in the endometrium. The *cervix uteri* is inflamed and the cervical canal is more or less obliterated and tightly contracted. The *cornua uteri* appear normal in the gross structure. In the lumen of the uterus, throughout its entire length, a considerable mucopurulent discharge is present. Some areas show pus undergoing caseation without marked foul odor. The uterine tubes are dilated to 6 mm. throughout their entire length. The walls are thick and fibrous. At the isthmus the dilation forms a definite pus pocket, being 2 cm. in diameter and extending upward on the tube 3 cm. The fimbriated ends are adherent to the broad ligament. In the lumen there appears a mucopurulent exudate. This purulent material is odorless. The left ovary is firmly adherent to the uterus by fibrous attachments which extend from the body to the horn. It averages 6-8 cm. in diameter. The capsule is slightly thickened. On its inner border there is a large, persistent *corpus luteum.* The central portion of the ovary is cystic. The cyst measures approximately 4 by 5 cm. in diameter. The right ovary is very irregular in outline, and is comparable in size to the left. A sagittal section shows only a small amount of normal ovarian tissue. Centrally located and surrounded by ovarian tissue is an abscess, the content of which is greenish yellow and pasty in consistency. The pus is putrid, having a stale, pungent odor. The ovarian tissue forms a wall 1¼ cm. thick around the abscess. At the inner periphery and separated from the abscess by a slight constriction and wall of connective tissue, is a small cyst containing a straw-colored serous fluid. The cyst is 1 cm. in diameter, oval in shape, and enveloped by a hard but thin fibrous wall.

2. *Microscopical description.*—The endometrium of the uterus shows a partially exfoliated epithelium, only shreds remaining in which the nuclei are barely visible. That which remains intact is normal except for the frequent presence of leukocytes, and is composed of a simple columnar epithelium. Many uterine glands are cystic. The cysts are three or more diameters larger than the normal glands and are made up of an outer wall composed of dense connective tissue fibers. These support, in a few places, a single layer of epithelial cells of low columnar type. Degeneration of this epithelium is pronounced. In the cystic cavity very little cellular material appears, only a few polymorphonuclear leukocytes and mononuclear leukocytes and a small amount of fibrin can be seen. Similar inflammatory cells

extend into the cystic wall. Uterine glands in the vicinity of those which are cystic show atrophy, due to an overgrowth of connective tissue. This also appears in other areas where no cysts are seen. The epithelium of many glands is entirely atrophied and replaced by proliferations of young connective tissue cells. The stroma in general shows a high degree of inflammatory reaction, there being quite universally present, polymorphonuclear leukocytes, lymphocytes, plasplasma cells, and fibroblasts. In some areas these are collected so as to form small abscesses. The myometrium shows similar but less extensive cellular infiltration. The serosa is normal. The uterine tubes show a normal serosa. The muscular coat is atrophied at the expense of connective tissue proliferations. The epithelium of the mucosa is simple columnar, and is exfoliated in some areas. Where exfoliation appears the cells are degenerated and only a homogenous, eosin-staining, fibrin-like material remains. In the *tunica propria,* there are masses of polymorphonuclear leukocytes closely packed so as to form small abscesses in the wall. The lumen contains dense masses of leukocytes, mostly polymorphonuclear, and small mononuclear cells, among which plasma cells are occasionally seen. Some fibrin is also present. Necrosis of the inflammatory elements has commenced in the central portion. The medulla of the right ovary consists for the most part of fibrous connective tissue. Several areas show collections of leukocytes, mostly polymorphonuclear and mononuclear cells. In some places these form small abscesses. In the cortex the stroma is very vascular. In one section there appears an atretic follicle. One section shows a cystic follicle, with the *theca folliculi* greatly thickened. Only remnants of the *stratum granulosum* remain. Many of the nuclei of this layer are pyknotic.

3. *Bacteriological findings.*—

(1) Uterus and uterine tubes	(a) *Staphylococcus epidermidis* (Gordon)
	(b) *B. coli communis*
	(c) *B. pyogenes* (Lucet)
	(d) *Streptococcus mitis* (Alpha type)
(2) Right ovarian abscess	(a) *Staphylococcus aureus* (Rosenbach)
	(b) *Streptococcus mitis*
3. Right ovarian cyst	(a) Sterile.

4. *Diagnosis and discussion.*—1. Purulent cervicitis, metritis, and salpingitis. 2. The uterus shows evidence of chronic changes, such as fibrosis and cystic glands in the endometrium. 3. Right ovarian abscess, with chronic inflammation of right ovary. 4. Small follicles

showing cystic and atretic degeneration are also seen. 5. *Corpus luteum* cyst of left ovary. These changes support the diagnosis of incurable sterility. Infection most likely entered through injury at time of breeding and gradually proceeded to involve the entire genital tract.

CASE 3

Clinical history.—Beauty Frances, Holstein cow, 2 years old, delivered a dead full-term calf following severe dystocia on September 23, 1920. Traction necessary to make delivery. Placenta came away normally. Developed severe purulent metritis within five days after parturition. Parauterine abscesses soon developed, the larger of these being located on the superior surface of the vagina between the left side of the uterus and the rectum, in the pelvic cavity. This measured approximately 8 inches in length by 4 in width. Small abscesses over the external wall of the uterus could be palpated, the size of which varied from that of a pea to that of a walnut. The ovaries were also enlarged and thought by rectal palpation to contain abscesses. The large abscess was evacuated on October 13, 1921. From this ½ liter of thick creamy pus streaked with blood was obtained. On October 23, 1921, the abscess was again evacuated. The pus this time was similar, but brown in color and had an offensive odor. Cultures were prepared from the purulent exudate, from which the following organisms were isolated: (a) *B. pyogenes* (Lucet), (b) *Streptococcus anginosus* (Beta type). At this examination another abscess over the left horn and extending to the ovary was palpated. This was not opened. The animal became emaciated, showed slight intermittent fever, and loss of appetite. The lesions became progressively worse and slaughter was advised on December 17, 1920.

Necropsy

1. *Gross description.*—The cervix and *corpus uteri* are drawn downward to the left owing to the adhesions and weight of the abscesses. The cervix appears normal. The body of the uterus is 3 cm. in length and its mucosa appears normal. The right uterine horn and right ovary are drawn downward and backward. An abscess is present on the right horn, 9 cm. anterior to the *corpus uteri.* This involves the perimetrium. The abscess is 3 cm. in diameter. The right horn is adherent in many places to the rectum and colon. The carunculae are dull white in color. They measure from 1 to 15 mm. across the surface and rise to a height of from 3 to 5 mm. from the gland mucosa. The gland mucosa is inflamed. There is no accumulation of pus in this horn. The left uterine horn proceeds forward and outward over a large abscess, to which it is firmly adherent. It

turns abruptly at a distance of 10 cm. anterior to the body of the uterus, the turn forming an angle of 45 degrees. Very few carunculae appear in the first portion of the horn. They become more numerous in the anterior half. Below the horn and adherent to it is a large abscess which measures 14 cm. in length and 10 cm. in width. Smaller secondary abscesses are present on the surface of the larger one. The abscess wall is thick and fibrous and its contents are thick, pasty, and malodorous. The abscess is adherent to the pelvic wall and colon. The right *tuba uterina* is normal. The left *tuba uterina* enters the large abscess at a distance of 4 cm. from the tip of the horn. As it enters the abscess it is lost to view. The right ovary measures 4 cm. in length, 3 cm. in width, and 2 cm. in depth. It contains a *corpus luteum* measuring 2.5 cm. in diameter. The center is cystic. Ventral to the *corpus luteum*, in the ovarian stroma, there is a cyst, measuring 17 mm. in diameter. Many Graafian follicles appear on the surface of the organ. The left ovary is buried in the large abscess from which it can not be differentiated.

2. *Microscopical description.*—The cervix appears normal. The uterus shows a quite uniform degeneration of uterine glands. This change is especially marked in the glands nearer the lumen of the organ. The epithelium of the glands shows granular degeneration of the cytoplasm, with only remnants of cells remaining. The nuclei are markedly pyknotic. Some show a marked infiltration with lymphocytes. The epithelium of the mucosa is in most places desquamated. In the lumen of the organ is occasionally seen an exudate, consisting of inspissated serum, lymphocytes, and large mononuclear cells. There is an increased activity on the part of the mucosa of the right uterine tube. Considerable mucus appears in the lumen, together with marked losses of epithelium. A few lymphocytes appear in the lumen which also infiltrate the mucosa. The right ovary presents many Graafian follicles which show marked cystic changes. These range in size from very small follicles to those measuring from 2 to 3 mm. in diameter. The nuclei of cells of the *membrana granulosa* are markedly pyknotic. The *liquor folliculi* instead of being very light, is precipitated as dense, homogenous, deep eosin-staining material. An example of this is illustrated in Figure 3. Sections of the wall of the large cyst show it to be of an edematous, thick, supporting, connective tissue structure. The *theca folliculi* and *membrana granulosa* are flattened out through great distention of the follicle. The primitive follicles appear normal. In one section there is also present a small *corpus luteum* cyst. This is approximately 1 mm. in diameter. The central portion is composed of a deep eosin-staining, homogenous, coagulated

fluid. The inner border is composed of lutein cells supported by connective tissue and remains of the *theca folliculi*. *Corpora albicantia* are numerous throughout the ovarian cortex. Sections of the wall of the large abscess show the wall to be composed externally of dense collagen fibrils. Toward the inner wall the connective tissue becomes more fibrillar. This shows quite a uniform infiltration with polymorphonuclear leukocytes, large mononuclear leukocytes, and plasma cells. The inner portion is almost entirely composed of exudative cellular material supported by young connective tissue fibers.

3. *Bacteriological findings.*—
   (1) Body of uterus, sterile
   (2) Right *cornu uteri, B. pyogenes* (Lucet)
   (3) Left *cornu uteri,* sterile
   (4) Right uterine tube, sterile
   (5) Right ovary, sterile
   (6) Abscesses (a) *B. pyogenes* (Lucet)
   (b) *Streptococcus anginosus* (Beta type).

4. *Diagnosis and discussion.*—
   1. Mild chronic metritis
   2. Catarrhal inflammation of right uterine tube
   3. Cystic degeneration of Graafian follicles and small *corpus luteum* cyst in right ovary
   4. Periuterine and parauterine abscesses, with abscess formation about the left uterine tube and left ovary.

The persistence of infection about the uterus without involvement of that organ to any marked extent, is remarkable. The presence of large periuterine abscesses would undoubtedly lead to permanent sterility through adhesions, even tho the genital organs themselves remain comparatively free from infection. The changes in the Graafian follicles may be the result of inflammation or disturbed uterine function. This is not known.

CASE 4

Clinical history.—Pauline, Holstein cow, 2 years old. Last pregnancy terminated September 6, 1920, with a premature delivery of the fetus. The fetus was coated with a yellowish brown, semi-turbid, tenacious exudate. The placenta was retained and removed 24 hours following parturition. Rectal examination and palpation of genital organs on October 23 revealed a large abscess, the size of an orange, in the left ovary. This was evacuated through the vagina. The cow suffered considerable shock following the operation and lactation became diminished for a number of hours. Had symptoms of severe abdominal pains, and loss of appetite for twelve hours. Gradually returned to normal. Examined on November 2, the abscess had again

enlarged with marked adhesions between left ovary and uterine horns. The abscess became larger very rapidly, with development of marked adhesions throughout the pelvis. Animal was regarded as incurably sterile and owner was advised to slaughter. Cultural studies of the purulent exudate were made from time to time. The bacterial flora consisted of (a) *B. pyogenes* (Lucet), (b) *Staphylococcus candidus* (Cohn), and (c) *Streptococcus fecalis* (Alpha type). The animal was slaughtered on December 7, 1920.

Necropsy

1. *Gross description.*—Carcass is poorly nourished. There is an abscess 28 by 23 cm. situated in the left pelvic cavity. This is adherent to adjacent muscles, broad ligament, uterus, left ovary, intestines, and peritoneum. It is well encapsulated and easily separated from its attachments. The walls are thick, and within them is a large quantity of pus. The pus is partly caseous and partly liquified. The odor is extremely offensive. The vagina is normal. The cervical canal of the uterus also appears normal. The right *cornua uteri* runs in a normal direction forward, downward, and outward, and the tip of the horn is curved backward to the *corpus uteri*, where the ovary is attached. The right horn and the body of the uterus contain no pus. The carunculae are very prominent. The tips are deeply congested, and measure 13 by 8 mm. across the surface. They rise from the gland mucosa, on the average, 4 mm. The left uterine horn proceeds in an irregular manner forward and outward. It then turns upward and again downward, over a large parauterine abscess. It coils itself about this abscess and adheres closely to it. The tip of the cornua is pressed between the two abscesses and is lost to view in the inflammatory overgrowths. There is no pus in the lumen. The carunculae are large and appear inflamed. They average in size, across their flattened surface, 6 by 12 mm. and extend upward from the surrounding mucosa from 2 to 3 mm. The right *tuba uterina* is normal in appearance. The left is not visible because of extensive abscess formation about it. The right ovary appears normal. It measures 3 cm. in length, 1.5 cm. in width, and 1 cm. in depth. The left ovary is buried in the abscesses which have formed about it so that it is completely lost to view. The abscesses on the left horn, not included in the parauterine abscesses previously described, are two in number. One lies beneath the horn and the other anterior to it. The former is 12 by 15 cm. in size, and the latter 6 by 8 cm. These abscesses and both horns are adherent to the pelvic walls, colon, and rectum.

2. *Microscopical description.*—The cervix is normal. The mucosa of the uterus is in the resting stage. The glands, for the most part, are very small. There appears to be in some areas an overgrowth

of connective tissue, and in other areas the walls are edematous. There is an increase of lymphocytes, mononuclear leukocytes, and plasma cells in the stroma of the gland mucosa. In the acini of some of the glands, lymphocytes are present. A few peripheral glands show degeneration of the epithelium. The right uterine tube is practically normal. In the right ovary there are many degenerating Graafian follicles. The cells of the *membrana granulosa* are partly degenerated, the nuclei of which show pyknosis and karyorrhexis. The *liquor folliculi* is replaced by a more heavily precipitated fluid. It appears homogenous and is deeply stained with eosin. In some follicles where ova appear, the cells of the *cumulus oöphorus* are degenerated similar to those of the *membrana granulosa.* In the ovum the cytoplasm appears to have undergone a hyaline degenerative change. Other areas show small cysts lined by lutein cells. These are small cystic remains of *corpora lutea. Corpora albicantia* are numerous.

3. *Bacteriological findings.*—
   (1) *Corpus uteri,* sterile
   (2) *Cornua uteri,* sterile
   (3) Right uterine tube, sterile
   (4) Right ovary, sterile
   (5) Parauterine abscess
      (a) *B. pyogenes*
      (b) *Streptococcus fecalis* (Alpha type)
      (c) *B. proteus*
      (d) *Staphylococcus candidus* (Cohn)
   (6) Periuterine abscesses, same except no *B. proteus* isolated.
4. *Diagnosis and discussion.*—
   (1) Mild non-purulent metritis
   (2) Cystic degeneration of Graafian follicles of right ovary
   (3) Periuterine and parauterine abscesses

The absence of bacteria in the genital organs cultured is comparable to the results obtained in case 3. The infective process seems to be completely localized with ability of the mucosa of the genital tract to withstand the invasion of the organisms. This immunity from attack, no doubt, would not be permanent, for sooner or later the progress of the infection would lead to definite changes in the uterus and right uterine tube, such as have already occurred in the left uterine tube and left ovary. The cystic degeneration of medium sized Graafian follicles, whether of importance or not, is at least an interesting observation.

CASE 5

Clinical history.—Aged Holstein cow, Lady Astrea. Calved normally in 1919, aborted April 15, 1920. Retained placenta was followed by a severe metritis. She was three months recovering from this. No treatment was administered after the placenta was removed. Examined October 13, 1920, and pronounced incurably sterile. Slaughtered October 29, 1920.

Necropsy

1. *Gross description.*—The carcass is well nourished. The cervical canal is tightly closed, but does not appear inflamed. The body of the uterus and horns is thickened. The mucosa of the uterus is not inflamed. The carunculae are normal. The right uterine tube is adherent to the right horn of the uterus. The uterine tube is enlarged, especially pronounced at the fimbriated end, and near the uterine end it appears normal. The tube is very tortuous at the fimbriated end. It is dilated to 1 cm. in diameter, and contains a clear straw-colored fluid. The lumen is crossed by interlacing bands, giving it a multilocular appearance. The tube winds its course through a mass of connective tissue, which in some places is so dense that it can not be definitely seen. Near the uterine end the tube is 2 mm. in diameter. At the fimbriated extremity, there appears an abscess, adherent to the uterine tube and right ovary. It measures 2 cm. in diameter, and is completely encapsulated within a thin wall. The pus it contains is not malodorous, is pasty in consistency, and greenish yellow in color. The left ovary is 4 cm. in length and 2.5 cm. in width. On the surface there are many small follicles, and buried in the substance of the ovary, there is a large *corpus luteum.* It is 1.5 cm. in diameter at the surface of the ovary and extends into its substance 13 mm. The right ovary is approximately 3.5 cm. in length and 2.5 cm. in width. It is encapsulated by a firm connective tissue capsule. The ovary is very hard and the cut surface shows no visible ripe follicles, except at one border, where a small portion of normal appearing ovarian tissue is seen. The intestines and mesentery are firmly adherent to the right ovary.

2. *Microscopical description.*—The cervix is normal. The uterus is normal. The uterine mucosa is in the resting stage, as shown by the small inactive glands. The left *tuba uterina* is normal. The right *tuba uterina* is normal at the isthmus. Sections across the tube near the ampulla show a tube with a greatly thickened wall, due to proliferation of the connective tissue. There is also fibrous thickening of the mucous folds. This has formed adhesions between the folds, leaving gland-like structures enclosed within masses of connective tissue. These structures are lined with a low cuboidal epithelium

and contain precipitate of serous fluid and mucin. Some have become greatly dilated by the retained fluid. In the center the fibrosis has been so complete that the attachments extend across the lumen and connect with similar areas on the opposite side. Some of the mucous folds do not appear to have undergone much thickening, but in places are elongated and flattened out. Throughout the areas of fibrosis, and in the lumen of the dilated structures, there are lymphocytes and occasionally polymorphonuclear leukocytes. The inflammatory cells are, however, not numerous. The left ovary shows many small cystic Graafian follicles. The *membrana granulosa* is mostly degenerated, and the *liquor folliculi* is replaced by a thick, dark-staining, homogeneous material. Some of the follicles show another type of degeneration, as pictured in Figures 1 and 2. These show a greatly thickened *theca folliculi* and proliferated epithelial cells of the *membrana granulosa* and may be interpreted as atretic follicles. Some sections show small cystic *corpora lutea*. Surrounding the wall is seen connective tissue, lying within which is an area resembling the *corpus albicans*. The innermost portion of the wall is composed of a thin layer of lutein cells. The content of the cyst is not rich in albumin or mucin, for the precipitate is light and granular. The right ovary shows similar cystic changes of the Graafian follicles. The most evident lesion, however, is the marked increase of connective tissue, leaving a sclerotic organ. Sections through the abscess show a dense capsule of connective tissue. Toward the innermost portions the cells of the exudate are closely packed. Polymorphonuclear leukocytes predominate, with plasma cells and large clear mononuclear leukocytes rather numerous.

3. *Bacteriological findings.*—
   (1) *Corpus uteri,* sterile
   (2) Right *cornu uteri, B. pyogenes* (Lucet)
   (3) Right *tuba uterina*
      (a) *Staphylococcus candidus* (Cohn)
      (b) *Streptococcus ignavus* (Alpha type)
      (c) *B. pyogenes* (Lucet)
   (4) Right ovary, sterile. Cyst, *B. pyogenes*
   (5) Left *cornu uteri,* sterile
   (6) Left *tuba uterina,* sterile
   (7) Left ovary, sterile
   (8) Tubal abscess
      (a) *B. pyogenes* (Lucet)
      (b) *Streptococcus ignavus*

4. *Diagnosis and discussion.*—
   (1) Hydrosalpinx of right *tuba uterina*
   (2) Abscess of fimbria of right *tuba uterina*
   (3) Sclerosis of right ovary, with cystic degeneration of many Graafian follicles
   (4) Cystic degeneration of Graafian follicles of left ovary

The fact that sterility existed in this case with only obstruction of the uterine tube on the right side indicates the close relationship between ovary and sterility. Evidently the ova in the left ovary were degenerated when set free, or the pathologic condition of the right side prevented fertilization and implantation of the ova from the left ovary.

CASE 6

Clinical history.—Holstein cow, 12 years old. Calved normally December 7, 1919. Bred January 20, 1920; April 7, 1920; July 17, 1920. No history of disease. Examined October 13, 1920. The examination showed hydrosalpinx in both uterine tubes, and both ovaries large and cystic. The animal was pronounced incurably sterile and slaughtered October 29, 1920.

Necropsy

1. *Gross description.*—The carcass is well nourished. The cervix is partially dilated. It appears normal in structure except for small cysts which appear deep in the structure of the internal *os uteri.* A small tumor projects from the outer surface of the body of the uterus. It is 2 cm. in diameter and is located in the muscular coat of the uterus, and gives the rounded prominence seen on the serosa of the *corpus uteri.* The growth is soft, circumscribed, and pink in color. The mucosa of the uterus appears normal. The right uterine tube begins as a normal structure. It gradually enlarges until it reaches a diameter of 1.5 cm. The tube is hard, and runs a markedly tortuous course. It contains a thin straw-colored fluid in its lumen. The lumen is for the most part obliterated and replaced by interlacing strands of tissue giving it a multilocular appearance. At the fimbria the tube is adherent to the right ovary. The left uterine tube presents the same picture as the right, except that it is smaller and not adherent to the ovary at the fimbriated extremity. The right ovary is 3 cm. in length and 2 cm. in width. It is hard and fibrous in appearance, and is covered by a firm, hard capsule. In the center of the ovary there is a large persistent *corpus luteum.* It measures 1.5 cm. in diameter. The outer wall is yellow in color (2 mm. thick), and the center presents a hard dark red mass which is not adherent to the lutein tissue of the wall. The central mass is from 0.5 to 1 cm. in

diameter. The left ovary is comparable in size to the right one. It contains a *corpus luteum* and appears normal.

2. *Microscopic description.*—The cervix shows a normal mucosa. The internal portion adjacent to the *corpus uteri* has many cystic glands deep in its wall, surrounded by the myometrium. The largest of the glands is 1.5 cm. in length and 1.5 cm. in width. The cystic glands are lined by simple cuboidal epithelium, and the outline is very irregular. The precipitated content of these cysts is in most instances very small in amount, but in one it is dense, homogenous, and eosin-staining. The epithelium of the uterine mucosa, in some places, appears thicker than normal. This is evident both in the cornua and in the *corpus uteri.* The epithelial cells are flat instead of columnar, in these areas, and are several layers in thickness instead of simple. Adjacent to these apparently squamous cell and thickened epithelial areas, the cells are simple columnar in type. This may be interpreted as "ectodermoisering," described by Wall. The uterus appears normal in every other respect. Sections through the tumor, described in the wall of the *corpus uteri,* show it to be composed of smooth muscle, well circumscribed by connective tissue. The gland mucosa is in a resting state. Sections through the enlarged *tubae uterinae* show a comparatively thin wall, consisting almost entirely of connective tissue. The mucous membrane consists of a greatly flattened simple cuboidal epithelium. The folds of the mucosa are stretched and converge toward the center where the connective tissue is much more pronounced, giving the central convergent folds great thickness. In this, collapsed adherent folds are completely surrounded by edematous connective tissue and appear as acini of glands. The adherent folds give the tube an appearance of multilocular cysts, all lined by the same type of low epithelium. They contain a faintly hematoxylin staining material indicating its mucinous composition. Inflammatory cells are not numerous and when present consist of lymphocytes. The ovaries are sclerotic. Primitive Graafian follicles are very few in number, and *corpora albicantia* are very numerous. A few Graafian follicles show degenerative changes characterized by flattening and stretching of the *membrana granulosa* to a single layer of cells and replacement of the *liquor folliculi* by a more dense material having the staining reaction of mucin.

3. *Bacteriological findings.*—

(1) *Os uteri externum*
- (a) *Staphylococcus aureus* (Rosenbach)
- (b) *Staphylococcus aurantiacus* (Schröter)
- (c) *B. coli communis*

(2) *Corpus uteri.* Same as *os uteri externum*
(3) Right *cornu uteri,* sterile
(4) Left *cornu uteri,* sterile
(5) Right and left *tuba uterina,* sterile
(6) Left and right ovaries, sterile

4. *Diagnosis and discussion.*—
(1) Cystic uterine glands in wall of *os uteri internum*
(2) Leiomyoma in body of uterus
(3) "Ectodermoisering" of uterine epithelium (Replacement of simple columnar by stratified ectodermal, in some areas)
(4) Hydrosalpinx, both uterine tubes
(5) Sclerotic ovaries, with cystic degeneration of most medium sized and large Graafian follicles

Sterility in this case would have been absolute with only the presence of bilateral hydrosalpinx. In this, even tho clinical history is not complete, in all probability a puerperal infection followed the last parturition. This, then, may be theoretically considered as the starting point of the infection which left in its wake the irreparable pathologic changes in the uterine tubes. The cystic changes in the ovaries may or may not have significance. The leiomyoma was not sufficiently large to cause sterility had other portions of the genital tract been normal.

CASE 7

Clinical history.—Aged Holstein cow. Last parturition about September, 1918. Suffered retained placenta. Came to our attention October 19, 1920. Diagnosed chronic cervicitis with hypertrophy of external *os uteri.* Deep seated *corpus luteum* in right ovary. Cultures prepared at this time from cervix obtained from swabs showed the following flora: (a) *B. pyogenes,* (b) *B. coli,* (c) *Staphylococcus aureus,* (d) *Staphylococcus aurantiacus. Corpus luteum* removed from right ovary and cervix painted with Lugol's solution on October 30, 1920, again on November 10 and December 18, 1920. On January 10, 1921, removed a large portion of hypertrophied cervical folds, at which time also a quantity of pus was located in the uterus. The left horn was hard upon palpation. Adhesions were also noted between ovaries and uterus at this examination. Another examination on February 28, 1921, revealed a continued marked cervicitis and purulent metritis. The right ovary was the size of a lemon, and firm upon rectal palpation. The animal was pronounced incurably sterile and slaughtered March 5, 1921.

Necropsy

1. *Gross description.*—The carcass is poorly nourished. There is a large quantity of muco-purulent discharge in the vagina. The walls of the vagina are inflamed. There are two cysts in the floor of the vagina, 2 cm. in diameter. These contain a thick mucinous material. The folds of the external *os uteri* are hypertrophied. Granular, inflammatory areas, pin point in size, stud the mucous surface. The cervical canal contains much thick yellow pus. The mucosa of the body of the uterus is rather dry. The right horn of the uterus is hard and indurated and about one-third smaller than the left one. At the bifurcation of the uterus, situated above and to the right, is an adhesive mass of tissue, adherent to the serosa of the horn. At this place the wall is hard and thick. This horn contains a considerable quantity of white pus, which is creamy in consistency. The wall of the right horn is 1.5 cm. in thickness. The left uterine horn is flatulent and indurated. The wall is 1.5 cm. in thickness. It contains pus, as does the right side of the uterus. The right uterine tube is normal at the isthmus. At a distance of 2 cm. from the uterus it becomes very tortuous. It gradually enlarges until it reaches 1 cm. in diameter. It is distended with a clear serous fluid. The fimbriated end is obliterated by a mass of connective tissue. This mass is 10 cm. in width, 4 cm. in depth, and 7 cm. in length. It is covered by mesenteric fat which adheres to it and brings a loop of the small intestine in close apposition. In the center of this connective tissue mass there is considerable pus. The connective tissue first described forms the wall of the abscess. This wall is adherent to the right ovary on one side, and to the serosa of the uterus on the other side. The abscess extends into the right ovary and is responsible for its large size. The pus in the ovarian abscess is greenish, thick, and pasty, and has a nut-like odor. The left uterine tube is enlarged, and the walls are thick and hard. The right ovary is covered by dense connective tissue, being almost completely buried in the mass. It measures 7 by 3 cm. It contains an old *corpus luteum* 2 cm. in diameter. The ovary appears sclerotic. The left ovary is normal. It measures 5 by 3 by 1.5 cm. It contains a *corpus luteum* 1.5 cm. in diameter. Many small Graafian follicles are also present.

Microscopic description.—The epithelial lining of the vagina is stratified ectodermal. The outer portion shows some destruction of epithelial cells, but not pronounced. The inflammatory exudate seen grossly in the vagina is evidently drainage material from the uterus. Lying on the epithelial surface, many polymorphonuclear leukocytes are seen. The cyst described grossly is composed of a lining of simple columnar epithelium, thrown more or less into folds (Bartholin gland).

The cavity contains a faint neutral-staining, homogenous material, probably mucus. Throughout this material cholesterin clefts and fatty acid crystals are numerous. Tiny globules of neutral fat are also seen. The *cervix uteri* shows extensive superficial proliferation. This has in many instances occluded the openings of the cervical folds so that gland-like structures without outlet to the surface appear buried beneath this proliferated connective tissue. The cells of these occluded folds contain much mucus, as do also the epithelial cells of the surface mucosa. In the zone of fibrosis, many small capillaries are seen, and quite uniformly infiltrating the area are plasma cells and large mononuclear leukocytes. The body of the uterus and the cornua show marked changes in the mucosa. The lining epithelium is very irregular in its state of preservation. In one area, for a short distance, the epithelium appears as stratified ectodermal six to eight cells in thickness. It ends abruptly and is continued on each end as simple columnar epithelium. The columnar epithelium contains much mucus but the "ectodermoised" area is free of this secretion. Attached to the epithelium and infiltrating it there remain occasionally polymorphonuclear leukocytes. In some places the epithelium is necrotic. Beneath the epithelial surface the mucosa is densely infiltrated with leukocytes. Plasma cells predominate, with polymorphonuclear leukocytes and lymphocytes also numerous. They diminish in number in the deeper structures of the mucosa and young connective tissue cells become more prominent. The uterine glands are markedly atrophied. In many places the inflammatory reaction has produced proliferative changes occluding the outlet of the glands. This has resulted in dilation with retention of mucus. These have very irregular and tortuous outlines. The epithelium is low cuboidal and is not seriously damaged. Some glands show a greatly flattened epithelium surrounded by rather dense fibrillar connective tissue, and in the lumina of many, polymorphonuclear leukocytes are seen. Throughout the myometrium there are several collections of cellular infiltrations similar in character to those described for the endometrium. The mucosa near the tips of the horns is much less involved. Many normal glands still remain but superficial changes have begun which suggest the gradual transition to the chronic changes as described for the other portion of the uterus. In the left *tuba uterina* the wall is thickened, owing to the increase of connective tissue. The folds of the mucosa are greatly thickened, and many adhere to one another. In the central portion of the lumen the folds converge where they have become adherent to folds on the opposite side of the tube. Owing to this overgrowth, many folds have been brought together at their base, so that they appear as acini of glands below the connective tissue mass. All

the folds, even where adherent, are still lined by simple columnar epithelium, which contains much mucus. The connective tissue is infiltrated with lymphocytes, and in the lumina between adherent folds, polmorphonuclear leukocytes and lymphocytes are occasionally found. The right *tuba uterina* is normal at the isthmus. Above this the tube is large. The wall is much thicker and edematous. The folds of the mucosa are thickened and elongated. They converge toward the center of the lumen where they form a thick mass of edematous connective tissue, lined by simple columnar epithelium. The other folds are likewise covered by the same type of epithelium. Considerable exudate is present in the lumen of the tube and between adherent folds. This consists of inspissated serum, fibrin, and a few polymorphonuclear leukocytes and lymphocytes. The ovaries show a marked lymphocytic infiltration, which in some areas forms dense masses. The larger follicles show cystic changes, marked only by increased density of *liquor folliculi.* The smaller follicles show quite uniformly degenerative changes in the ova and the cells of the *membrana granulosa.* These changes are not marked and are difficult to interpret.

3. *Bacteriological findings.*—
   (1) The *os uteri externum,* and uterus
      (a) *B. pyogenes* (Lucet)
      (b) *Streptococcus non-hemolyticus II* (Gamma type)
      (c) *Staphylococcus aureus* (Rosenbach)
   (2) Uterine tubes. Right tubo-ovarian abscess and right ovary
      (a) *B. pyogenes*
      (b) *Streptococcus non-hemolyticus, II*
      (c) *Staphylococcus epidermidis* (Gordon)
   (3) Left ovary, sterile
4. *Diagnosis and discussion.*—
   (1) Vaginitis and cystic Bartholin glands
   (2) Chronic purulent cervicitis and metritis
   (3) Hydrosalpinx of both tubes
   (4) Right tubo-ovarian abscess
   (5) Right ovary sclerotic, cystic Graafian follicles
   (6) Left ovary shows cystic Graafian follicles

The presence again of cystic degenerative changes in the Graafian follicles is interesting. As a result of the long continued metritis, chronic changes have occurred which have left the uterus in a state of irreparable destruction with loss of breeding efficiency. The causes of sterilty are apparent.

CASE 8

Clinical history.—Holstein cow, 4 years old. Last calf born February 19, 1919, normal. Did not retain placenta. Cow has never aborted. Infectious abortion in herd five years ago. Cow has regular estrous periods. Animal was bred twelve times following birth of calf in February, 1919, and at no time did conception take place. Slaughtered as a tuberculin reactor December, 1920. No evidence of tuberculosis found at postmortem examination.

Necropsy

1. *Gross description.*—The vagina is normal except near the vulva where there is evidence of granular venereal disease. The cervical canal is open, it being possible to insert the small finger without difficulty. The uterus appears normal on its serous surface. Both uterine tubes are normal. The left ovary is normal in size. A *corpus luteum* 2 cm. in diameter is imbedded in the ovarian substance. It is hemorrhagic, many small blood vessels being present about the periphery. Two large follicles 15 mm. in diameter are present on the surface. These appear to be cystic. The right ovary is normal in size. On the upper surface there appears a cyst 1 cm. in diameter. The walls are thick. A small scar (*corpus albicans*) appears on the border of the cyst.

2. *Microscopical description.*—The vagina is normal. The cervix is normal. In the uterus the superficial glands of the mucosa are active, appearing according to Marshall's descriptions as in the period of proestrum. These glands show degeneration and desquamation of the epithelium and increased cellular and mucous exudate in their lumina. The cells of the exudate are mostly lymphocytes and large mononuclear leukocytes. Erythrocytes are not evident outside the blood vessels. The deeper glands are normal and in a state of rest. The *tubae uterinae* are normal. The ovaries appear for the most part normal, the primitive ovarian follicles are normal, as also are the larger ones that are present in the several sections taken.

3. *Bacteriological findings.*—

(1) *Os uteri externum, corpus uteri,* and right horn
  (a) *Staphylococcus aureus* (Rosenbach)
  (b) *Staphylococcus aurantiacus* (Schröter)
  (c) *Staphylococcus candidus* (Cohn)

(2) Left uterine horn, uterine tubes, and ovaries are sterile.

4. *Diagnosis and discussion.*—In this case the only suggestions of pathological changes are obtained from study of the endometrium. The changes seen do not, however, seem commensurate with absolute

sterility. Possibly altered secretion, which can not be judged histologically, played an important part. Nutritional disturbances may also have been an exciting factor. Any hypothesis proposed can have no scientific support in the light of present knowledge. Cases such as these are difficult to account for. The possibility of the *corpus luteum* of the left ovary influencing conception must also be taken into account, the enucleation of which might have cleared up the condition.

CASE 9

Clinical history.—Aged Hereford cow. Several calves were born normally, after which the animal failed to conceive. Had been sterile one year when brought to our attention. Clinical examinations revealed nothing but cervicitis. This condition was treated regularly with Lugol's solution for two or three months. *Corpora lutea* were enucleated from time to time. Slaughtered because of sterility on December 15, 1920.

Necropsy

Gross description.—The carcass is well nourished. The external *os uteri* shows many hypertrophied folds. The cervical canal contains a thick tenacious discharge. This is transparent and glistening. In some places it is streaked with blood. In the wall of the *corpus uteri* there is a tumor 13 mm. in diameter. It is rounded and well circumscribed. The mucosa of the uterus is normal. The walls are 8 mm. in thickness. The right uterine tube appears normal. It contains a white colored tenacious mucus. The left uterine tube is normal except at the fimbriated end, where it is adherent to the left ovary. The tube here is slightly dilated as in hydrosalpingitis. The right ovary contains many Graafian follicles. These, instead of containing a clear serous fluid, contain a mucinous one. Ovaries are normal in size. A *corpus luteum* is embedded in the ovarian substance. The *corpus luteum* is surrounded by a tough capsule, except in a small area at the surface where a small portion protrudes from the surface. The *corpus luteum* is 2 cm. in irregular diameter. In the center is a cystic cavity 4 mm. in diameter, containing a clear fluid. Over the remainder of the surface of the ovary there are many Graafian follicles. A *corpus luteum* lies on the broad ligament. It measures 1.5 cm. in diameter and is very hard in consistency. This represents a recently enucleated *corpus luteum* which is being absorbed in the peritoneal cavity.

2. *Microscopical description.*—The cervix is normal. The uterus is practically normal. A few glands of the mucosa show dilation and a flattened epithelium surrounded by rather dense circular bands of connective tissue. In others and surrounding some, lymphocytes are

seen. The glands are in a beginning state of activity. The tumor described in the wall of the *corpus uteri* is composed almost entirely of smooth muscle. It is well encapsulated. The left *tuba uterina* is normal except at the fimbriated end, where it is dilated and adherent to the ovary. The folds of the mucosa are adherent near their tips and the spaces formed between them are lined with low cuboidal epithelium. The folds are greatly stretched and thin. This gives the tube the appearance of small multiple cystic cavities. There is a precipitate in the lumina, between the folds, indicating the previous presence of a serous exudate. Only occasional collections of lymphocytes are seen in the exudate. Figure 8 illustrates this condition. The right *tuba uterina* is normal. The left ovary contains many *corpora albicantia.* The medium sized follicles are cystic, as indicated by the replacement of the normal *liquor folliculi* by a fluid precipitating much albumin and containing much material staining like mucin. Other follicles show atretic degeneration. Primitive Graafian follicles are very few in number, and the organ appears to be sclerotic. Sections obtained from the wall of the small cyst of the *corpus luteum* show it to be composed internally of a flattened layer of lutein cells, supported by a loose connective tissue framework. This is derived from ingrowths of connective tissue into the *corpus luteum* from the supporting membrane of the Graafian follicle. Beneath this the solid cords of lutein cells, with rich blood supply, are seen. The central cavity contains a small amount of debris, precipitate of the fluid it contained. Sections of the enucleated *corpus luteum,* found in the peritoneal cavity, show a uniform necrosis of all lutein cells. These appear as granular eosin-staining areas without definition. Small clear spaces left by neutral fat are abundant. The right ovary shows cystic and degenerated follicles as described for the left one. It also appears somewhat sclerotic. Some of the ovarian arterioles show hyaline degeneration of the media.

3. *Bacteriological findings.*—
   (1) *Os uteri externum, Staphylococcus epidermidis* (Gordon)
   (2) Right *cornu uteri, Streptococcus mitis* (Alpha type)
   (3) *Corpus uteri,* left *cornu uteri,* uterine tubes, and ovaries are sterile.
4. *Diagnosis and discussion.*—
   (1) Leiomyoma of *corpus uteri*
   (2) Hydrosalpinx of abdominal osteum of tube with adhesions to right ovary
   (3) Sclerotic changes in ovaries, and cystic degeneration of follicles
   (4) Persistent *corpus luteum* in left ovary, with central cystic degeneration.

Sterility in this case can only be accounted for histologically by the hydrosalpinx in the right *tuba uterina,* sclerotic changes in ovaries, and cystic degeneration of ovarian follicles. The persistent *corpus luteum* which formed so frequently in the left ovary was also a contributing factor. The changes seen indicate a one-time virulent infection, leaving only as a result the changes in the right *tuba uterina* and possibly the altered ovarian function. The case exemplifies further the close relationship that exists between the ovaries and sterility, involvement usually being bilateral.

CASE 10

Clinical history.—Holstein cow, about four years old. Presented at clinic for examination July 24, 1920. Past breeding unknown. The vagina was inflamed and the walls were adherent. This created a blind ending, just anterior to the urethral opening. The right ovary was found to be cystic. The cyst was approximately the size of an English walnut. This cyst was ruptured several times. The right uterine tube was enlarged, and thought to be affected with hydrosalpingitis. In the left ovary a *corpus luteum* was palpated. This was enucleated on September 1, 1920. It was impossible to dislodge it before, owing to deep embedding. Animal appeared in estrum September 3, 1920, but was not bred because of the occluded vagina. Was condemned as incurably sterile and slaughtered for food purposes December 17, 1920.

Necropsy

1. *Gross description.*—Carcass exceptionally well nourished. The vagina is closed just anterior to the urethral orifice. The stricture appears to be the result of an inflammatory reaction which brought the vaginal walls in close apposition and united them by scar tissue. The center of the stricture presents a small rounded opening which communicates with the anterior portion of the vagina. The opening is 3 mm. in diameter. Anterior to the stricture the vagina has narrowed to 1.5 cm. in width. The cervix appears normal. The vagina enlarges at the external *os uteri* so that this structure is easily accommodated. The body of the uterus is normal. The left horn of the uterus is 3 cm. in cross-diameter, at a point just anterior to the body. The right uterine horn is 5 cm. in diameter in the respective area, and continues to its extremity to be approximately twice as large as the left one. The right horn is flaccid. The uterine mucosa appears normal. The right *tuba uterina* is normal at the isthmus. It gradually enlarges until it reaches a diameter of 8 mm. at the fimbriated extremity. This enlarged area adheres to the right ovary. It contains a clear, watery, straw-colored fluid. The lumen is crossed by

strands of the mucosa which are adherent to one another, giving the lumen a multilocular appearance. The left *tuba uterina* is normal. The right ovary measures 5 cm. in length, 4 cm. in width, and 3 cm. in depth. It appears cystic. A large cyst about 2 cm. in diameter is present. It contains a clear straw-colored fluid, which coagulates upon leaving the cyst. The wall of the cyst is 4 mm. in thickness. The inner border is yellow, while the outer portion appears white. The yellow portion is 2 mm. in thickness. This represents the remains of lutein cells from a *corpus luteum* which passed through cystic degeneration instead of normal absorption. (This *corpus luteum* cyst was broken per rectum several times, and each time re-formed). The left ovary is normal in size. It contains on its surface 3 large Graafian follicles 6 mm. in diameter. There is also a *corpus albicans* on its surface measuring 2 mm. in diameter.

2. *Microscopical description.*—Over the mucosa of the vagina and adherent to it, there is considerable inflammatory exudate consisting of desquamated epithelial cells, large mononualear leukocytes, and lymphocytes and fibrin. The epithelium is intact in most places, only occasionally appearing irregularly exfoliated. Beneath the epithelium is a uniform distribution of lymphocytes and plasma cells, and occasional normal lymph follicles. The remainder of the wall appears normal. The cervix appears normal. The *corpus uteri* shows an extensive atrophy of mucous glands and a dense fibrous tissue replacement. Only occasionally are glands seen. Lymphocytes infiltrate the mucosa quite uniformly, more numerous than normal. In the cornua the epithelium is in many places necrotic and in others entirely lost. The glands of the mucosa show degeneration as evidenced by loss of epithelium, and lymphocytic infiltration into the lumina. This may correspond to proestrum as described by Marshall, but the destruction seems too extensive not to be considered pathological. The stroma of the endometrium is edematous. Glands do not appear atrophied, but simply show degenerative changes. In the lumen of the cornua there is considerable cellular debris, consisting of desquamated epithelial cells, lymphocytes, and mononuclear leukocytes. The left *tuba uterina* is normal. The right *tuba uterina* is normal at the isthmus. At the ampulla it becomes dilated and corresponds histopathologically to the descriptions previously given for hydrosalpinx. The walls are thickened to a great extent. The mucous folds do not cross the lumen, but are all flattened out and incorporated in the wall, with entire loss of epithelium. A few normal appearing folds remain. The enlarged lumen is lined by a simple flat epithelium (stretched columnar epithelium). The right ovary contains many *corpora albicantia.* Some follicles show degenerative changes. In

one the *membrana granulosa* and the *theca folliculi* have greatly atrophied, only remnants of these layers remaining. The ovum is caught in and surrounded by proliferations of connective tissue, which extend along the side formerly occupied by the *cumulus oöphorus*. In this area lymphocytes are numerous. Many follicles appear normal, while some medium sized ones appear cystic. These contain a heavy homogeneous eosin-staining precipitate, in place of the normal *liquor folliculi*, and the *membrana granulosa* is flattened out. Small primitive follicles are not numerous but appear normal. The wall of the cystic *corpus luteum* is lined by an edematous connective tissue, beneath which a thick layer of lutein cells are seen, supported by dense connective tissue. The left ovary is practically normal.

3. *Bacteriological findings.*—
   (1) *Os uteri externum, corpus uteri,* left *cornu uteri,* uterine tubes and ovaries are sterile
   (2) Right *cornu uteri, Staphylococcus epidermidis* (Gordon)
4. *Diagnosis and discussion.*—
   (1) Stricture of vagina resulting from vaginitis
   (2) Chronic proliferative changes in uterus with atrophy and degeneration of uterine glands
   (3) Hydrosalpinx of right *tuba uterina*
   (4) Many atretic and cystic degenerated Graafian follicles in right ovary
   (5) Cystic *corpus luteum* in right ovary

The presence of staphylococci in the right *cornu uteri* can not be regarded as responsible for the changes seen. It can best be defined as a chance invader, and not at the time of necropsy playing a pathological rôle. Sterility in this case would have been absolute with only the presence of vaginal stricture, so great were the bands of attachment. The uterine changes and hydrosalpinx are, as is the vaginal change, too, the end result of chronic infection produced most likely by streptococci or *B. pyogenes* or both. The degenerative changes described for the right ovary are interesting, but possibly not an important contribution.

CASE II

Clinical history.—Scrub cow, about 3½ years old. Animal was used as a control in the abortion herd at University Farm. Purchased from South St. Paul, May 20, 1918. Age at that time, 8 months. Agglutination test for infectious abortion in June, 1918, positive at 1-20, and slight at 1-50. September 1, 1918, test positive only at 1-20. Bred December 30, 1918. Pronounced pregnant February 15, 1919. Examined for pregnancy April 7, 1919. Found not pregnant. The animal was seen to have considerable blood on rear quarter two weeks previous

and was considered to have aborted. Large *corpus luteum* in right ovary was enucleated. Bred June 2, 1919. Pronounced pregnant October 23, 1919. Agglutination test for infectious abortion on November 22, 1919, was negative. A calf was born normally March 4, 1920. Agglutination test March 9, 1920, negative. Bred May 10, 1920. Pronounced pregnant August 11, 1920. Agglutination test August 13, 1920, negative. A calf was born normally February 15, 1921. Agglutination test on calf and dam was negative February 15, 1921. The calf died February 18, 1921. The cow developed a discharge from the uterus after parturition. This continued until she was slaughtered on March 4, 1921. The animal was condemned as a tuberculin reactor and as metritis had followed the last parturition, opportunity was taken for pathological and bacteriological study.

Necropsy

1. *Gross description.*—The carcass is well nourished. The mucosa of the vagina is slightly inflamed. The vagina contains a large quantity of thick, viscid, mucous discharge which is streaked with pus. The cervical canal is dilated and contains much discharge similar to that seen in the vagina. Otherwise it appears normal. The *os uteri internum* is inflamed. The body of the uterus is deeply congested. The horns of the uterus are deeply congested and each contains thick mucus, which in some places is streaked with pus. The pus is thick and yellow. The carunculae are large and prominent. The surfaces of the carunculae range from 0.5 to 2 cm. in diameter. They rise from the gland mucosae from 3 to 6 mm. The uterine tubes are normal. The ovaries are small, but appear normal.

2. *Microscopical description.*—The cervix is normal. The uterus shows considerable exudate in the lumen, lying on the epithelial surface. The exudate consists of inspissated serum, mucus, polymorphonuclear leukocytes and lymphocytes. Many desquamated epithelial cells are also present in the exudate. In the epithelium there are many polymorphonuclear leukocytes. The epithelial cells contain much mucus. The epithelium is simple columnar in type. Beneath the epithelium collections of leukocytes are numerous. These are for the most part polymorphonuclear, but lymphocytes are also numerous. The uterine glands are normal and in a state of rest. Occasional leukocytes are seen in the lumina of these glands. The blood vessels are engorged with blood. The uterine tubes are in a state of congestion. Some hemorrhage into the lumen exists. The right ovary is normal. Primitive and medium-sized follicles are numerous and appear normal in structure. In the left ovary, in the sections studied, several follicles appear in a state of atretic degeneration. Others show

a changed *liquor folliculi,* the coagulum being dense, homogeneous, and eosin-staining. Other structures of these follicles are normal. Very few normal Graafian follicles appear in the sections studied.

3. *Bacteriological findings.*—

(1) *Uterus* (a) *Streptococcus viridans* (Alpha type)
(b) *Staphylococcus epidermidis* (Gordon)
(c) *Staphylococcus aureus* (Rosenbach)
(d) *Sarcina lutea*
(e) *Torula rosea*

(2) Uterine tubes, sterile

(3) Ovaries, sterile

4. *Diagnosis and discussion.*—This can not be regarded as a case of sterility, for the animal was not sterile. It was studied in this series as an illustration of mild puerperal metritis. The left ovary shows cystic degeneration of many ovarian follicles, others being atretic. It is not known of what significance such change may be.

CASE 12

Clinical history.—Holstein cow, 7 years old. When 2 years old she gave birth to a normal calf. Since that time she has been sterile. Had irregular periods of estrum and when bred did not conceive. Animal was condemned because of sterility and slaughtered for food March, 1921.

Necropsy

1. *Gross description.*—The carcass is well nourished. The vagina is normal. The cervix is normal. The body of the uterus is normal. In the left horn there is a very slight amount of mucopurulent discharge. The right horn is normal. The uterine tubes are normal. The left ovary is normal. The right ovary is normal. It contains a normal *corpus luteum* measuring 2.5 cm. in width and 1.5 cm. in depth.

2. *Microscopical description.*—The cervix is normal. The uterus shows a thickened epithelium which occurs only in places, portions adjacent to the thickened areas being normal. In the thickened areas the cells are flat and stratified to 6 or 8 layers in depth. This epithelium appears as stratified ectodermal and possibly corresponds to "ectodermoisering" described by Wall. The endometrium otherwise is normal, as are also the other uterine coats. The uterine tubes are normal. The ovaries are both equally involved. They present, in several sections studied, degenerative changes of the Graafian follicles. In one section a Graafian follicle is seen with the following changes: The *liquor folliculi* is replaced by a dense coagulum taking a neutral

stain. The epithelial cells of the *cumulus oöphorus* are mostly degenerated, a few cells of the *corona radiata,* however, still remain. The *zona pellucida* is dark in color, and the vitellus, instead of being granular and containing vacuoles, is replaced by a dense homogeneous neutral-staining substance. The nucleus is not present. The cells of the *stratum granulosum* are in a state of degeneration. Many are loosely distributed about the follicle. Nuclei show degenerative changes, for the most part pyknosis. Other Graafian follicles of medium size show the same dense coagulum replacing the normal light coagulum of the *liquor folliculi,* with stretching and flattening of the *stratum granulosum.* The *theca folliculi* is greatly thickened. Primitive ovarian follicles are numerous and appear normal. *Corpora albicantia* are numerous.

3. *Bacteriological findings.*—

(1) Cultures from the *cervix uteri,* uterus, *cornua uteri,* uterine tubes, and ovaries remained sterile.

4. *Diagnosis and discussion.*—In this case, as in cases 8 and 9, the etiology of sterility is not clear. The "ectodermoisering" described in the uterus does not seem a sufficient change to cause absolute sterility such as existed in this animal. The ovarian changes, cystic degeneration, and atretic degeneration, are the only histological changes throwing any light upon the possible etiology. But it can not definitely be agreed that this change is present in all follicles. All organs cultured were sterile. There may have been a mild puerperal infection following the birth of the calf, at two years of age. Certainly at the time of necropsy, no infection existed.

CASE 13

Clinical history.—Holstein heifer, 2 years old. Showed normal periods of estrum. Examination early in December, 1920, to determine inability to conceive, resulted in finding an occluded vagina and malformed uterus. This was thought to be a case of arrested development of the genitalia. The animal was closely bred, but not a twin. Condemned for sterility and slaughtered for food December 18, 1920.

Necropsy

1. *Gross description.*—The vagina is 5 cm. in length. A short distance anterior to the urethral opening the walls of the vagina come together, forming an almost complete stricture. In the center of the stricture is an opening 2 mm. in diameter. Anterior to this, the vagina enlarges slightly. There is no *cervix uteri.* From the vagina proceeding anteriorly, there are two hard and fibrous tubes contained within a common capsule. The length of these tubes, as they run parallel to one another, is 30 cm. They separate at this point

and proceed forward at angles to one another. At a distance of 14 cm. from the dividing point, they end abruptly. The centers of these tubes have lumina 4 mm. in diameter, which near the anterior extremity dilate to 1 cm. The largest diameter of each tube is 1.5 cm. At the anterior end of each tube there is a maldeveloped uterine horn. The right horn is larger than the left, and is nearly spherical. It measures 9 cm. in length and 10 cm. in cross diameter. The walls are very thin and the horn is distended with a yellow turbid fluid. The left horn is similar in appearance to the right one. Its measurements are 9 cm. in length and 5.5 cm. in cross diameter. The uterine tubes run backward from the tip of each horn, and end in an indistinct fimbria. The right ovary is slightly larger than the left. It measures 4.5 cm. in length and 2 cm. in width. Over the surface of the organ there are many small follicles. These, instead of containing a clear, watery *liquor folliculi,* contain an opalescent semi-solid fluid, probably an expression of small Graafian follicle cysts. The left ovary is also cystic and contains a *corpus luteum* 3 cm. in depth and 2 cm. in width.

2. *Microscopical description.*—Sections through the remains of the Müllerian tubes show a lining of low cuboidal epithelium, in most places simple, in some areas stratified. Beneath the epithelial surface the connective tissue is dense and consists for the most part of collagenous fibrils. A few large simple tubular glands are occasionally seen. The inner surface of the tubes is thrown into low, rounded folds. Smooth muscle is distributed throughout the connective tissue and is more abundant in the deeper structures. In the partially developed uterus the mucosa is lined throughout with a thick stratified ectodermal epithelium. Beneath this is a thick coat of connective tissue distributed evenly along the mucosa. This tissue is exceedingly edematous. The uterine glands lie beneath this coat of connective tissue. They are surrounded by dense connective tissue bands and the epithelium is low columnar. Some contain much mucus. The surface of the mucosa is thrown up into small irregular folds. Differentiation into gland mucosa and carunculae does not appear. The muscular coat is thin. The entire thickness of the mucosa does not exceed the ordinary development of the endometrium of a normal uterus. The uterine tubes appear normal in structure. In the ovaries medium sized Graafian follicles are exceedingly numerous. These show quite uniformly a *theca folliculi* of increased thickness, a quite normal appearing *stratum granulosum,* and a thick homogenous, neutral-staining coagulum of the *liquor folliculi.* In the several sections studied, no ova are present. Small primitive follicles are few in number.

3. *Bacteriological findings.*—

(1) Cultures prepared from the right *cornu uteri,* left *cornu uteri,* and ovaries, sterile

4. *Diagnosis and discussion.*—A case of absolute sterility from arrested development of the genitalia. Multiple cystic degeneration of the follicles, as described here, is frequently seen in the ovaries of young girls. These correspond histologically to the cystic changes described for ovaries in other cases herein reported.

CASE 14

Clinical history.—Holstein heifer, 2 years old. Showed normal periods of estrum. Examination early in December, 1920, in order to determine inability to conceive, resulted in finding an occluded vagina and rudimentary uterus. This was thought to be a case of arrested development of the genitalia. The animal was closely bred, but not a twin. Condemned for sterility and slaughtered for food, December 18, 1920.

Necropsy

1. *Gross description.*—The vagina is 7 cm. in length, the anterior extremity being completely closed. There is no *cervix uteri.* The vagina communicates anteriorly with two tubes, as in case 13. The tubes are contained within a common tough and fibrous sheath. The tubes themselves are very fibrous. The lumen is collapsed, and almost adherent from side to side. It does not communicate with the cavity of the uterus or vagina. The tubes continue forward as those described in case 13, each one ending at a partially developed uterine horn. The right uterine horn is 8 cm. in length and 4 cm. in cross diameter. The walls are very thin. The horn is distended to about half its capacity with a turbid, yellow, watery fluid. The left horn is extremely rudimentary. It measures 2.5 cm. in length and 1.5 cm. in cross diameter. The walls are thick and a yellow fluid is contained in the lumen. The right uterine tube is normal. The left uterine tube is short but appears normal. The right ovary is 5 cm. in length and 3 cm. in width. It contains a *corpus luteum* 24 mm. in width and 19 mm. in depth. Over the surface there are many small cystic follicles. The left ovary is 3 cm. in length and 2 cm. in width. It contains many small cystic follicles.

2. *Microscopical description.*—The persistent Müllerian tubes show a small lumen lined with stratified ectodermal epithelium supported by a dense connective tissue of collagenous type. Occasional glands are present in this area. Smooth muscle is distributed through the lower portion, but is not great in amount. The serosa is composed of a thick layer of areolar tissue. The partially developed *cornua uteri*

are similar in structure to those described for case 13. The uterine tubes are normal. The ovaries show many *corpora albicantia* distributed throughout the cortex. Primitive follicles are normal. Nearly all medium sized and large Graafian follicles show cystic degeneration, marked by a dense coagulum replacing the granular coagulum of the *liquor folliculi.* Ova are not seen in any of these follicles. The cells of the *stratum granulosum* do not appear to be damaged.

3. *Bacteriological findings.*—

(1) Cultures of the *cornua uteri,* uterine tubes, and ovaries remained sterile.

4. D*iagnosis and discussion.*—Partial arrested development of genital organs and cystic degenerative changes in Graafian follicles.

CASE 15

1. *Clinical history.*—Aged Holstein cow. A normal calf was delivered on November 20, 1920. The parturition was difficult owing to a breech presentation. Purulent metritis and cervicitis developed following parturition. On December 6, 1920, swabs were taken from the uterus and cultures prepared. From this material the following organisms were isolated: 1. *Bacillus pyogenes* (Lucet), *Staphylococcus aureus* (Rosenbach), and *Streptococcus pyogenes* (Beta type). On the same date a retained *corpus luteum* was palpated in the right ovary and enucleated. The right uterine horn was elongated and much enlarged, and a considerable quantity of thick yellow pus could be massaged from it. The cervix was also much inflamed. The uterus was flushed with a mild antiseptic and the cervix painted with pure Lugol's solution at ten-day intervals. Improvement was continuous and the animal was pronounced ready to breed on March 31, 1921. The periods of estrum were at this time regular. Animal apparently normal but not pregnant June 14, 1921.

2. *Diagnosis and discussion.*—(1) Purulent cervicitis and metritis, acute in type. and caused by *B. pyogenes,* and *Streptococcus pyogenes.* These organisms were found on three examinations. It will be interesting to note whether changes have been produced that will render the animal permanently incapable of reproduction. It is too early at this time to make a definite prognosis, except that clinically everything seems normal.

NOTE.—This animal is now pregnant from December 24, 1921, service.

CASE 16

Clinical history.—Aged Guernsey cow. Delivered a normal calf in June, 1920. The placenta was retained, following which she developed a severe purulent metritis. It received little attention until January 13, 1921, when examination revealed a deeply seated *corpus luteum* in the right ovary. The *cervix uteri* was inflamed and the

cervical canal partly dilated. The uterus was enlarged, flaccid, and abdominal in position. The persistent *corpus luteum* was enucleated on January 17, 1921. Following this operation the uterus began to contract, and within 24 hours 4 to 5 liters of thick, creamy pus was evacuated. The pus was very malodorous. Cultures were prepared from this discharging material. From this exudate the following organisms were isolated: (1) *B. pyogenes* (Lucet) and (2) *Streptococcus viridans* (Alpha type). Following the operation upon the *corpus luteum* the animal was very uneasy and failed to eat her evening meal. The discharging pus continued for 3 or 4 days. Examination on January 24 showed the uterus to be pelvic in location, almost normal excepting for a slightly enlarged right horn. The cervix was inflamed and was painted with Lugol's solution. The uterus was massaged. The animal was allowed to rest one month. On February 28 an examination showed the right horn of the uterus still slightly enlarged. The uterus was irrigated with a 2 per cent solution of therapogen. Examination on March 7 found all organs normal and cow showing symptoms of estrum. Discharged from the clinic March 9, 1921, apparently recovered. Examination in May revealed the development of a slight tubo-ovarian abscess. The animal was not pregnant.

2. *Diagnosis and discussion.*—Pyometra, cervicitis, and tubo-ovarian abscess, the etiology of which is (1) *B. pyogenes* (Lucet) and (2) *Streptococcus viridans* (Alpha type).

Note: This cow now (March 13, 1922) comes in heat regularly, discharge has ceased, and she is thought to be with calf.

CASE 17

1. *Clinical history.*—Holstein cow, about 5 years old. Normal calf was born November 15, 1920. Following parturition the placenta was retained. Purulent metritis developed but received no special attention until March 28, 1921. Examination revealed a much enlarged uterus (pyometra), cervicitis, cystic left ovary, and *corpus luteum* in right ovary. The cyst was ruptured and the *corpus luteum* enucleated on this date. Pus began to flow freely from the vagina within 24 hours after enucleating the persistent *corpus luteum*. The removal of the *corpus luteum* allowed the uterus to undergo normal involution. The pus which came from the uterus was yellow in color and streaked with blood and was very malodorous. Swabs were taken from the uterus and cultures prepared. The following organisms were isolated: (1) *B. pyogenes* (Lucet), and (2) *Staphylococcus epidermidis* (Gordon). The uterus was washed with a 2 per cent solution of therapogen on this date, and after being emptied, the entire organ could be placed beneath the hand, by rectal palpation. Examination on April 1, 1921, showed the uterus to have better muscular tone. The cervix was still

slightly inflamed. The cervix was treated with Lugol's solution. Examination on April 2 showed the animal to be in estrum. The left uterine horn was normal, the right uterine horn was still slightly inflamed. Examination on April 4 showed the left uterine horn to be practically normal, and the right horn still enlarged and flaccid. On this date the uterus was massaged and the cervix was treated with Lugol's solution. Examination on April 7 showed the right uterine horn to be smaller and with better muscular tone. The cervix was treated with Lugol's solution and the uterus washed with 2 per cent solution of therapogen. Following this it was massaged. On April 9, examination revealed a normal uterus, a *corpus luteum* in the left ovary, a contracted cervix, and a small quantity of pus in the vagina. The *corpus luteum* was enucleated. The animal appeared in estrum following this and was discharged from the clinic soon after.

2. *Diagnosis and discussion.*—Pyometra and cervicitis following parturition, and caused by *B. pyogenes* and *Staphylococcus epidermidis.* The animal has apparently recovered.

NOTE.—Later she was sold at public sale as a healthy individual.

CASE 18

1. *Clinical history.*—Holstein cow, 6 years old. Delivered a normal calf November 28, 1920. Following parturition the animal retained the placenta, but it was promptly removed. Following this the animal did not appear in estrum. While decumbent, a thick creamy discharge could be seen coming from the vagina. The animal was presented in the University clinic for treatment on March 28, 1921. Examination on March 28 revealed a large, elongated uterus, hanging down over the brim of the pelvis. In the right ovary was a large persistent *corpus luteum.* This was enucleated. On the following day the animal began to discharge large quantities of pus from the uterus. It was thick and creamy in consistency and light yellow in color. Swabs were taken from the uterus at this time and cultures prepared. The following organisms were isolated: (1) *B. pyogenes* (Lucet), (2) *Streptococcus viridans* (Alpha type), (3) Streptococcus (Gamma type), (4) *Staphylococcus aureus* (Rosenbach), and (5) *Staphylococcus epidermidis* (Gordon). The uterus gradually returned to normal. On April 22 a clinical examination of the genitalia was made. The right horn of the uterus was slightly enlarged and upon massage a small quantity of pus could be expressed. The uterus was washed with a 2 per cent solution of therapogen. On April 25 the uterus was found practically normal. The horns were of equal size. The organ was massaged per rectum until a clear mucus was discharged from the vagina. The cervix was still slightly inflamed and the cervical canal was partially open. The animal was pronounced

practically normal and discharged from the clinic on the following day. The animal has been bred and is now pregnant.

2. *Diagnosis and discussion.*—Pyometra and cervicitis caused by *B. pyogenes, Streptococcus viridans,* and staphylococci. Recovery has apparently been complete, but definite knowledge of this can not be had till later, when it is definitely known that a fetus has been carried through the normal period of gestation.

CASE 19

Clinical history.—Cow without clinical history, obtained from the abattoir at South St. Paul.

Necropsy

1. *Gross description.*—The vagina is normal. The cervix is normal. The right horn of the uterus is approximately 8 cm. in diameter, at a point just anterior to the *corpus uteri.* It is hard, upon palpation. It gradually tapers toward the tip of the horn. The lumen of the horn contains about 100 cc. of a yellowish, granular exudate. The mucosa (endometrium) and myometrium are extensively invaded with small yellow tubercles. Many are caseous and others calcified. On the mucous membrane these form small yellow, hard, rounded prominences. The left uterine horn is normal in size except near the tip, where there is a hard mass 4 cm. in diameter, and 2 cm. in length. This contains many small calcified tubercles. There is no exudate in the lumen of this horn. The right uterine tube is normal in appearance at the isthmus. Toward the ampulla it is dilated to 4 mm. and is very hard, upon palpation. It is yellow in color. The left uterine tube presents a similar involvement. The right ovary contains a cyst 17 mm. in diameter, and at the opposite end of the ovary, a large *corpus luteum.* The *corpus luteum* is 2 cm. in diameter. The center presents a cystic cavity 4 mm. in diameter. The left ovary is normal. There are many soft tubercles, gray in color, upon the broad ligament and surrounding the uterine tubes and ovaries. The mass is so dense that dissection of these organs from it is very difficult.

2. *Microscopical description.*—The uterus shows many tubercles throughout the wall, especially in the endometrium. The smaller ones have no central necrosis. These are composed of endothelioid cells and many giant cells are also seen. A zone of lymphocytes surrounds the tubercle. Larger ones are similar, with central necrosis. The stroma of the endometrium is infiltrated densely with lymphocytes. The glands are for the most part normal. A few are dilated, showing a thinned epithelium and fibrous thickening of the *membrana propria.* In the muscularis several large necrotic tuberculous masses are seen. The central portion shows extensive calcification, surrounding which

is a wide area of necrosis. Around the necrotic area are massed large numbers of endothelioid cells and many giant cells. Intermixed with and especially massed at the outer periphery there are numerous lymphocytes. The larger tubercles are well encapsulated with connective tissue. The larger tubercles of the muscularis extend also into the endometrium almost to the uterine epithelium.

Areas of the uterus where no tubercles appeared to be present grossly, are also normal microscopically.

The uterine tubes are practically destroyed by the tuberculous process. The tubes are slightly larger than normal. The mucosa is entirely destroyed. No normal structures remain. There is necrosis of all layers of the muscular coat. Around the necrotic material a thick layer of endothelioid cells is prominent, throughout which a few lymphocytes and fibroblasts are seen. A few giant cells are also present. The outer circular muscular fibers are still intact. Some sections show portions of tubal epithelium in a fairly good state of preservation, and others with necrotic remnants still present. In these areas there is extensive lymphocytic infiltration of the mucosa, with exudate consisting of coagulated serum and lymphocytes in the lumen. The serosa shows numerous tuberculous adhesions about it.

3. *Diagnosis.*—Advanced miliary tuberculosis of the uterine tubes, uterus, and parauterine tissues.

EXPERIMENTAL INOCULATIONS WITH *BACILLUS PYOGENES*

Two heifers were secured for experimental work with *B. pyogenes.* An attempt was made to infect these animals with recently isolated strains of the organism. Heifer No. 1 was in the eighth month of pregnancy, when 5 cc. of a serum bouillon culture of *B. pyogenes* from case 17 was introduced into the jugular vein (3 weeks before parturition). No observable symptoms of disease resulted. The animal carried the calf to maturity and two weeks after parturition the necropsy revealed a normal genital tract, free of bacteria. No other pathologic lesions were found. Heifer No. 2 was non-pregnant and 15 cc. of a bouillon culture of *B. pyogenes* from case 18 was introduced into the uterus. The animal developed no observable symptoms of disease and necropsy revealed a normal genital tract, practically free of bacteria. These cases illustrate the resistance of the normal body to infection, and the necessity of a predisposing cause. The prevalence of *B. pyogenes* in nature is not known. It must inhabit the animal's body and develop pathogenic characters when resistance for some reason is reduced. The inability to interfere with pregnancy is also noteworthy.

Laboratory animals were not inoculated with *B. pyogenes.* Time did not permit pathogenicity studies on small animals. The pathogenicity of *B. pyogenes* for laboratory animals has been thoroly demonstrated. According to Berger (61) and Holth (62), rabbits are the most susceptible of the small laboratory animals to experimental infection with *B. pyogenes.* Guinea pigs are less susceptible, and mice least so. Brown and Orcutt (48) were able to infect rabbits quite readily, the characteristic lesions produced being abscesses in various parts of the body.

SUMMARY AND CONCLUSIONS

1. BACTERIOLOGICAL

In the course of the bacteriologic investigations, standard works have been consulted for classification. Each organism was isolated in pure culture and then subjected to systematic study for identification. In the study of staphylococci the work of C. E. A. Winslow (54) et al, on "Notes on the Classification of the White and Orange Staphylococci," has been the basis of identification. Streptococci were at first identified according to Hollman's (55) classification and in the later work the identification was based solely on the reaction to blood agar. For the latter the monograph of James Howard Brown (56) has been followed carefully. In the studies on *B. pyogenes* the works of Lucet (46), Künnemann (47), Grips (52), Glage (53), and Ward (64) were consulted. For identification of *B. pyogenes* the work of Brown and Orcutt, "A Study of Bacillus pyogenes," has been the basis of classification (48). In addition to this, two rabbits were immunized with separate strains of *B. pyogenes.* Serum from these rabbits agglutinated all strains of the organism to an equal degree. The tables on pages 84 and 86 show the prevalence of organisms as they appear in the nineteen cases studied.

It is confusing in interpreting results in Table I to have such a large group of streptococci. All strains, excepting *Streptococcus pyogenes* and *Streptococcus anginosus* are of the non-hemolytic types (Alpha and Gamma). These two, however, fall into the group of hemolytic streptococci (Beta type).

It will be seen in careful study of the material presented that the organisms most important in infections of the genital tract of the cow are streptococci and *B. pyogenes.* These types are responsible for the greater number of infections. In all cases of severe non-specific metritis and other suppurative processes about the genitalia, *B. pyogenes* combined with streptococci, or the latter alone, have been isolated.

Other organisms are not regarded as playing a primary rôle. Unless the bacteriologic study is made during the progress of active infection, these types as well as others will most often not be found. In such cases one views only the results of infection, the active process having subsided. It is for this reason that in nearly all cases when no gross evidence of active inflammation exists, the genital tract is sterile. The vagina, *cervix uteri,* and *corpus uteri* must be excepted.

Organisms are not normally harbored as commensals in the internal genitalia of the cow, with exceptions as already made. Case 6 is an unparalleled example of this. Hydrosalpinx, the end result of active inflammation, existed, cultures from which were sterile. Case 10 also illustrates the point. Many other examples of a bacteria-free genital tract may be found in the case reports, and as compiled in Table I. The absence of *B. abortus* (Bang) supports the previous view, that it is not found in puerperal infections that persist for any length of time, and that it does not persist, so far as is known, in the genitalia of the cow. *B. abortus* was not isolated from any of the cases studied.

TABLE I

COMPILATION OF BACTERIOLOGIC RESULTS

Genital organ	Case number																		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Vagina	1 5 14	q	q	q	q	q	q	q	q	q	q	q	q	q	q	q	q	q	q
Os uteri externum	1 5 14	q	q	q	q	1 2 5	1 10 13	1 2 4	3	o	q	q	y	y	11 13	13 15	13 15	1 3 13 15 19	q
Corpus uteri	o	3 5 12 13	o	o	o	1 2 5	q	1 2 4	o	o	1 3 15 17 19	o	y	y	11 13	13 15	13 15	1 3 13 15 19	20*
Right cornu uteri	o	3 5 12 13	13	o	13	o	3 10 13	1 2 4	12	3	1 3 15 17 19	o	o	c	q	q	q	q	20*
Left cornu uteri	o	3 5 12 13	o	o	o	o	3 10 13	1 10	o	o	1 3 15 17 19	o	o	o	q	q	q	q	20*
Right uterine tube	o	3 5 12 13	o	o	4 9 13	o	3 10 13	o	o	o	o	o	q	o	q	q	q	q	20*
Left uterine tube	o	3 5 12 13	q	q	o	o	3 10 13	o	o	o	o	o	q	o	q	q	q	q	20*
Right ovary	o	2 12	o	o	o	o	3 10 13	o	o	o	o	o	o	o	q	q	q	q	q
Left ovary	q	o	q	q	o	o	o	o	o	o	o	o	o	o	q	q	q	q	q
Ovarian cysts	o	o	o	o	13	o	o	4	o	o	o	o	o	o	q	q	q	q	q
Ovarian abscess	y	2 12	y	y	13 9	y	3 10 13	y	y	y	y	y	y	y	q	q	q	q	q
Periuterine abscess	y	y	7 13	4 8 13 16	y	y	y	y	y	y	y	y	y	y	q	q	q	q	q

Explanation of Symbols in Table I

o—sterile
q—not cultured
y—structure not present
1—*Staphylococcus aureus*
2—*Staphylococcus aurantiacus*
3—*Staphylococcus epidermidis*
4—*Staphylococcus candidus*
5—*B. coli communis*
6—*B. coli communior*
7—*Streptococcus anginosus*
8—*Streptococcus fecalis*
9—*Streptococcus ignavus*
10—*Streptococcus non-hemolyticus*
11—*Streptococcus pyogenes*
12—*Streptococcus mitis*
13—*B. pyogenes*
14—*B. subtilis*
15—*Streptococcus viridans*
16—*B. proteus*
17—*Sarcina lutea*
18—*Torula rosea*
19—*Streptococcus* (Gamma type)
20—*B. tuberculosis**

*—stain only

CASE II

SUMMARY OF BACTERIOLOGIC RESULTS INCLUDING ALL CASES

Organism	Times found	Case number																		
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Streptococcus Alpha type	8	—	+	—	+	+	—	—	—	+	—	+	—	—	—	—	+	+	+	—
Streptococcus Beta type	2	—	—	+	—	—	—	—	—	—	—	—	—	—	—	+	—	—	—	—
Streptococcus Gamma type	4	—	—	—	—	—	—	+	+	—	—	+	—	—	—	—	—	—	+	—
B. pyogenes	9	—	+	+	+	+	—	+	—	—	—	—	—	—	—	+	+	+	+	—
Staphylococcus aureus	6	+	—	—	—	—	+	+	+	—	—	+	—	—	—	—	—	—	+	—
Staphylococcus all other types	10	—	+	—	+	+	+	+	+	+	+	+	—	—	—	—	—	—	+	—
B. coli	3	+	+	—	—	—	+	—	—	—	—	—	—	—	—	—	—	—	—	—
B. tuberculosis	1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	+*
B. proteus	1	—	—	—	+	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Sarcina lutea	1	—	—	—	—	—	—	—	—	—	—	—	+	—	—	—	—	—	—	—
Torula rosea	1	—	—	—	—	—	—	—	—	—	—	+	—	—	—	—	—	—	—	—

* *B. tuberculosis,* by stain; organs not cultured.

TABLE III

SUMMARY OF BACTERIOLOGIC RESULTS IN CASES OF SUPPURATION

Organism	Times found	Case number										Percent present
		2	3	4	5	7	11*	15	16	17	18	19†	
B. pyogenes	9	+	+	+	+	+	—	+	+	+	+	—	81.8
Streptococcus Alpha type	7	+	—	+	+	—	+	—	+	+	+	—	63.6
Streptococcus Beta type	2	—	+	—	—	—	—	+	—	—	—	—	18.1
Streptococcus Gamma type	3	—	—	—	—	+	+	—	—	—	+	—	27.2
Staphylococcus aureus	3	—	—	—	—	+	+	—	—	—	+	—	27.2
Staphylococcus other types	6	+	—	+	+	+	+	—	—	—	+	—	54.5
B. coli	2	+	—	—	—	+	—	—	—	—	—	—	18.1
B. tuberculosis‡	1	—	—	—	—	—	—	—	—	—	—	+	9.0
B. proteus	1	—	—	+	—	—	—	—	—	—	—	—	9.0

* Case 11, mild puerperal metritis of short duration; healing would probably soon have occurred.

† Case 18, tuberculous metritis and salpingitis.

‡ By stain only; cultures not made.

2. PATHOLOGICAL

The frequency with which one views degenerative changes in the ovaries of sterile cows can not be disregarded. It seems that in all cases of infection about the genital tract, multiple cystic degeneration of medium sized Graafian follicles is an almost constant finding. Until more study is made, especially on normal animals as controls, no definite statement can be made. The uterine tubes, because of their many folds and crypts and their delicate structure, offer the most favorable site for persistence of infection. Chronic changes in the genital tract are most frequent in this location and are usually seen in the form of hydrosalpinx. In the uterus chronic changes do not readily occur. Only after severe infection over a long period of time are sufficient changes produced to render the organ incapable of serving its natural use. It does not seem as readily susceptible to persistence of infection as do the uterine tubes. The changes noted in the uterus are fibrosis, cystic dilation of glands, atrophy of glandular epithelium, thickening of uterine epithelium, and various others. The *cervix uteri*, like the uterine tubes, offers a favorable site for bacterial reproduction. The folds of the mucosa are deep and in the crypts bacteria may gain entrance and multiply. Altho accessible to treatment, the deep crypts allow infection to persist, and often extend to other portions of the genital tract. Hypertrophy of cervical folds is the most constant chronic change. The vagina, because of its smooth stratified epithelial surface, is not readily infected. It may harbor pathogenic types of bacteria, as commensals, on its surface, in its accessory glands, in the subepithelial lymph follicles, or in the urethral orifice. It is suggested that the vagina and accessory structures may be the reservoir for organisms which infect the genital tract of the cow, including *B. abortus*, and other types which cause congenital (prenatal) infections. The route of infection may be through the lymphatic system, which is most highly developed about the female genital tract. The occurrence of parauterine and periuterine infections seems to support this view.

Nineteen cases have been studied and presented. The theory of infection does not explain all cases of sterility. Where no evidence of infection, past or present, exists, and the animal is sterile, the ovaries must be looked to as the cause of the condition, except of course, where malformation of the genitalia exists.

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Veterinary Obstetrics, W. L. Williams.
Veterinary Obstetrics (Fleming's), J. F. Craig.
Bovine Obstetrics, M. G. de Bruin.
Die Sterilitat des Rindes, E. Hess.
Epizootic Abortion in Cows, S. Wall.
Handbuch der vergl. mikroskop. Anat., W. Ellenberger.
Text-Book of Embryology, Bailey and Miller.
Text-Book of Embryology, C. W. Prentiss.
The Physiology of Reproduction, F. H. A. Marshall.
Sterility in Cattle, J. Albrechtsen.

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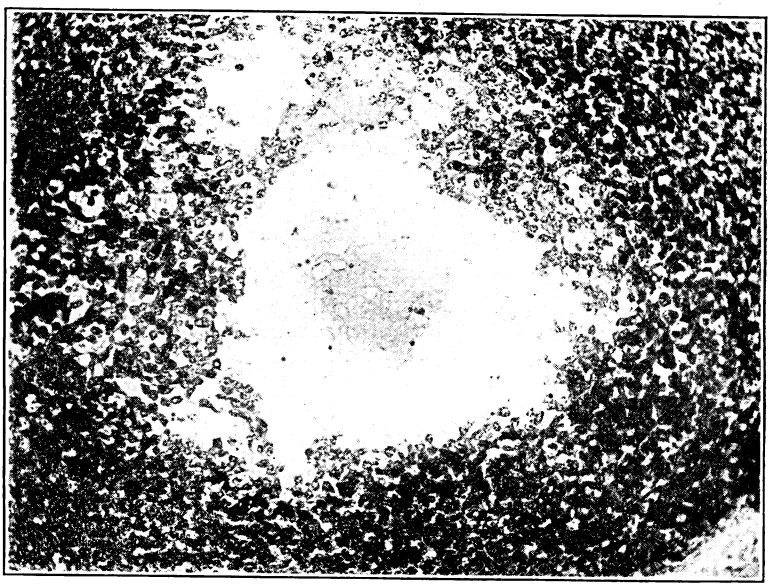

Fig. 1. Degenerative Change in Graafian Follicle, Case 5
Note proliferation of cells of *stratum granulosum*.

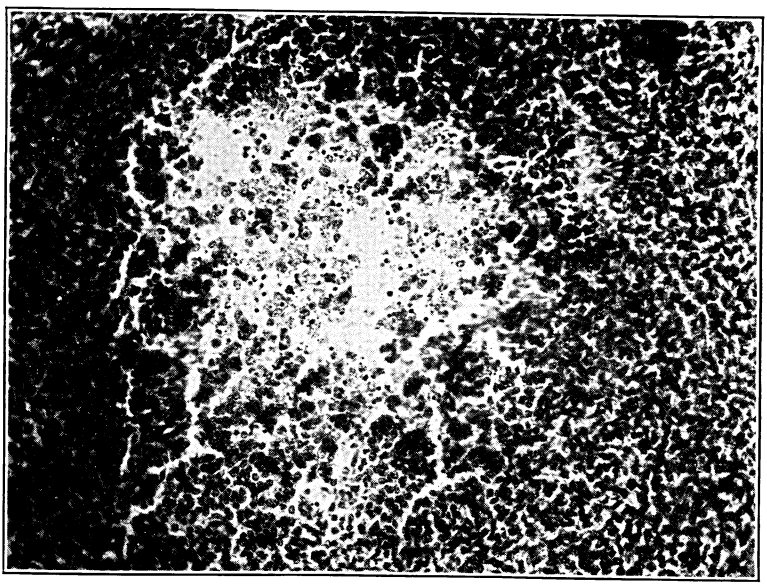

Fig. 2. Graafian Follicle Showing Degenerative Change, Case 1
Note thickening of *stratum granulosum* and *theca folliculi*.

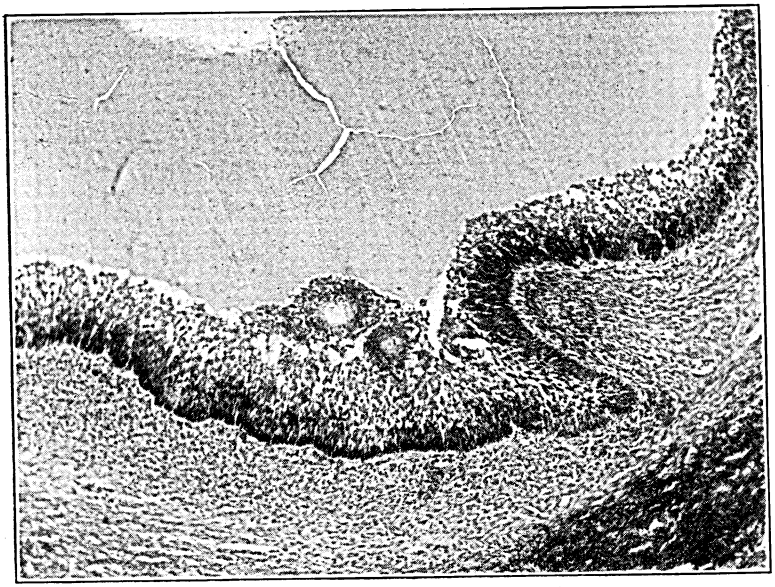

Fig. 3. Cystic Degeneration of Graafian Follicle, Case 5

Note dense coagulum replacing normal *liquor folliculi* and degenerative changes in cells of *stratum granulosum* (not marked in this case).

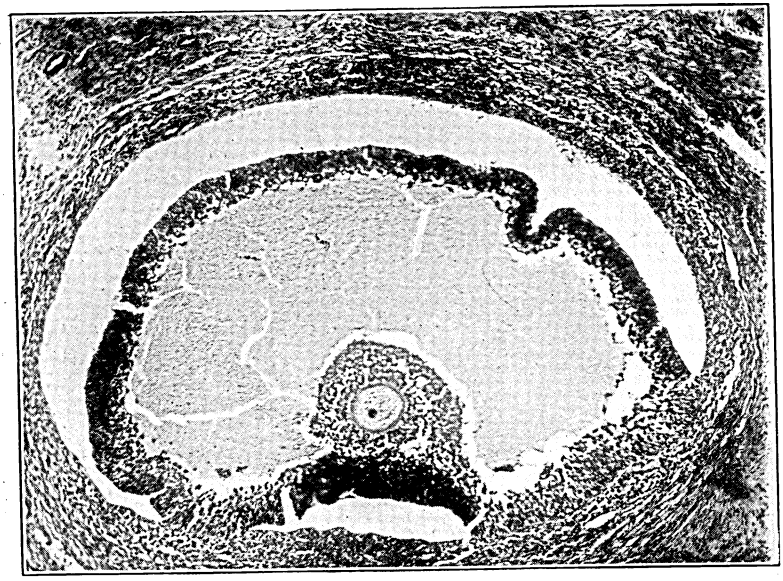

Fig. 4. Normal Graafian Follicle, Case 3

Note the granular character of the coagulated *liquor folliculi*. The pulling of the *stratum granulosum* from the *theca folliculi* is an artefact.

Fig. 5. Normal Follicle, Case 2.

Showing ovum surrounded by the cells of the *cumulus oöphorus*. Note the granular character of the *liquor folliculi* coagulum.

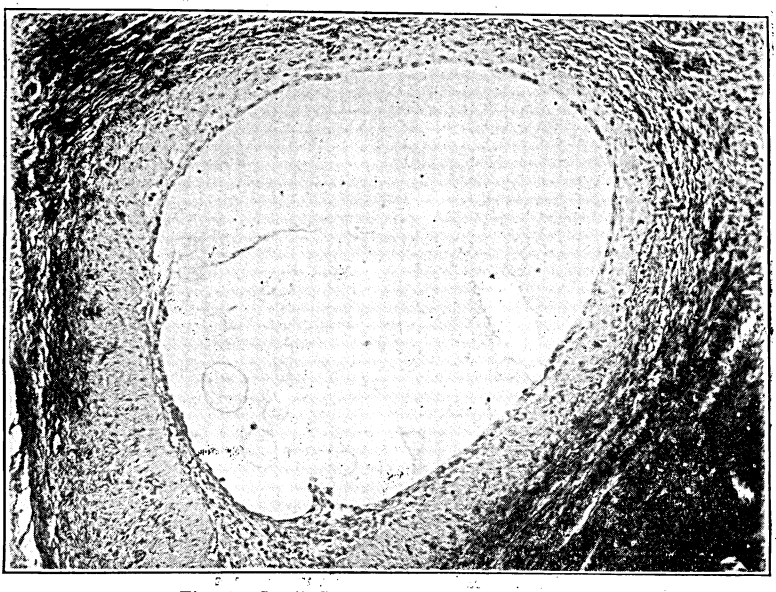

Fig. 6. Small Cystic *Corpus Luteum*, Case 5.

Lutein cells have undergone hyaline change. Cyst surrounded by *corpus albicans*. Fluid contains neutral fat.

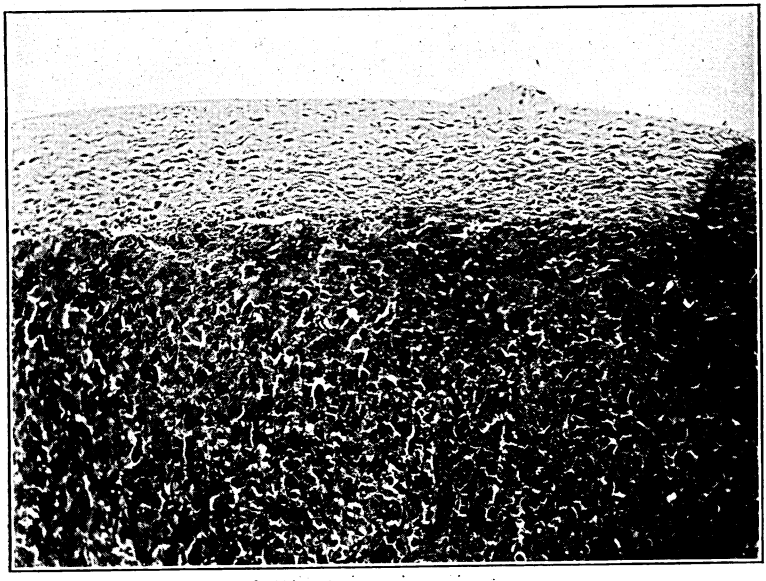

Fig. 7. Section Through Wall of Old *Corpus Luteum* Cyst, Case 10
Note connective tissue and lutein cells.

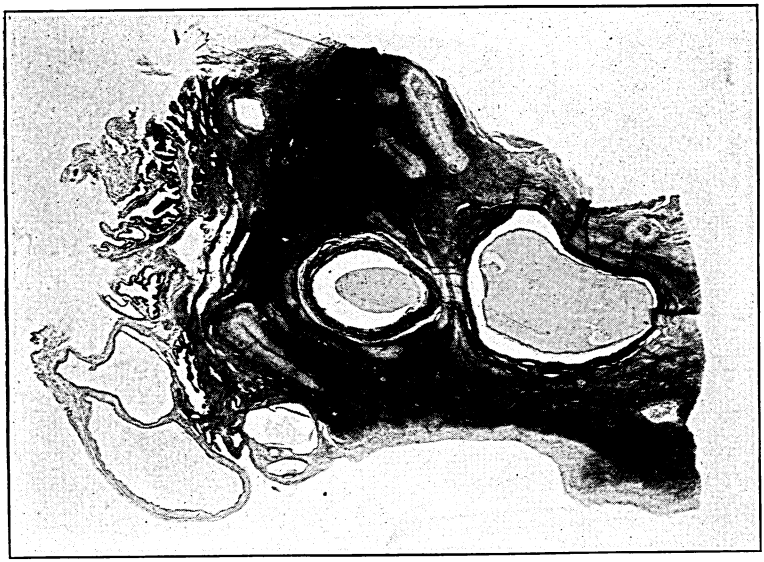

Fig. 8. Section Through Ovary, Case 9

Note uterine tube adherent to ovary, the multilocular cavities characterizing hydrosalpinx. Two Graafian follicles showing cystic degeneration are seen in the ovary.

Fig. 9. Low Power of Uterine Tube, Case 5
Hydrosalpinx, early stage.

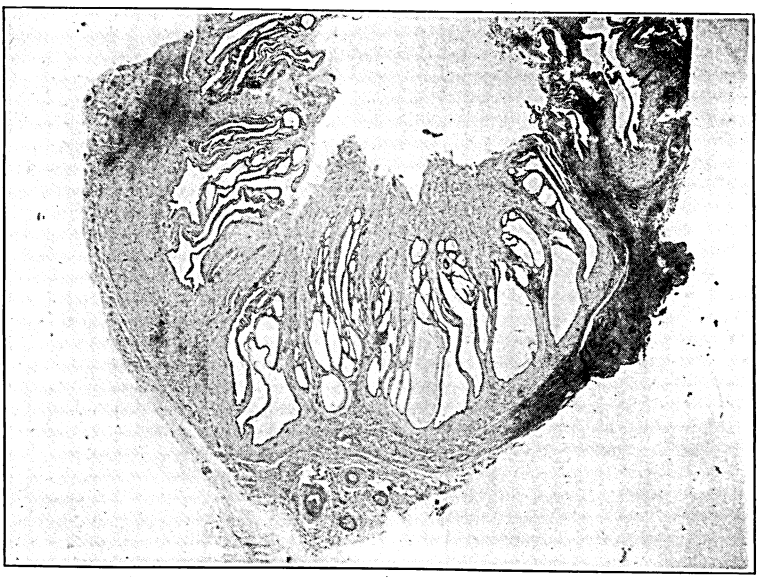

Fig. 10. Hydrosalpinx, Case 5

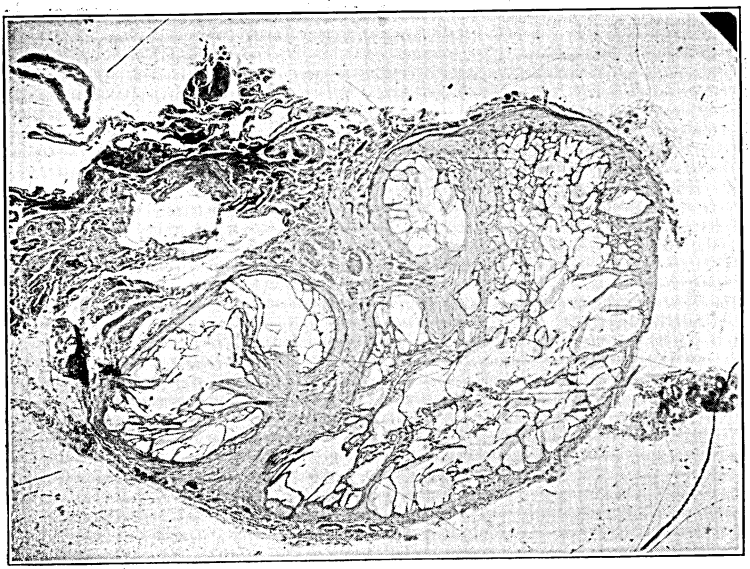

Fig. 11. Section Through Uterine Tube, Case 6
Hydrosalpinx, later stage. Note atrophy of many interlocking folds.

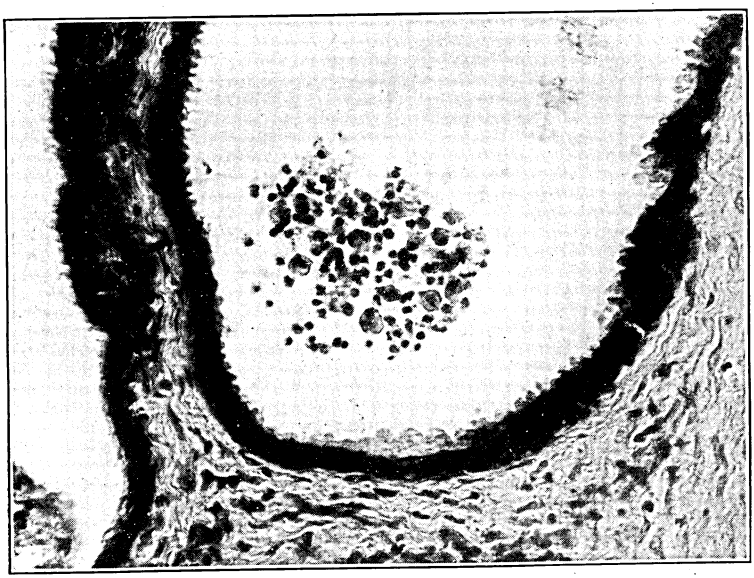

Fig. 12. Section Through One of the Cystic Pockets. Hydrosalpinx, Case 5
Note proliferation of connective tissue and epithelium. Exudate in lumen is composed of polymorphonuclears, lymphocytes and desquamated epithelium.

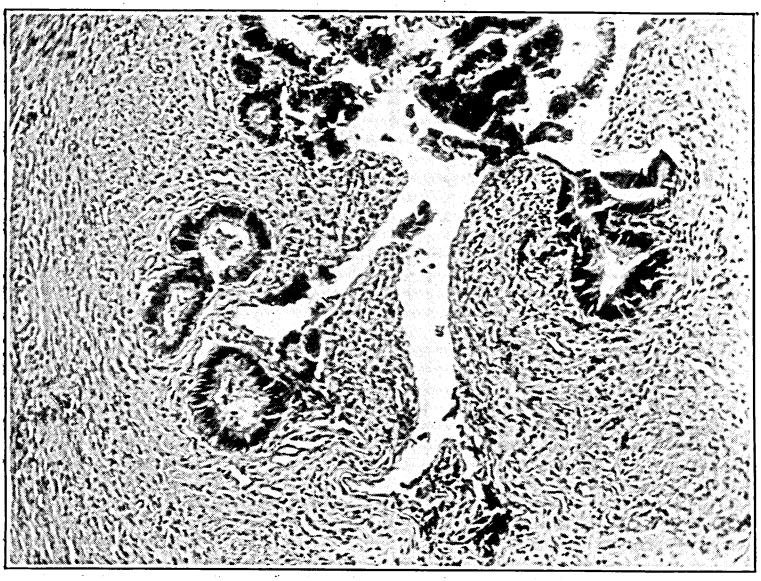

Fig. 13. Very Mild Salpingitis, Case 4

Epithelium is abnormally desquamated and in the wall many lymphocytes are seen.

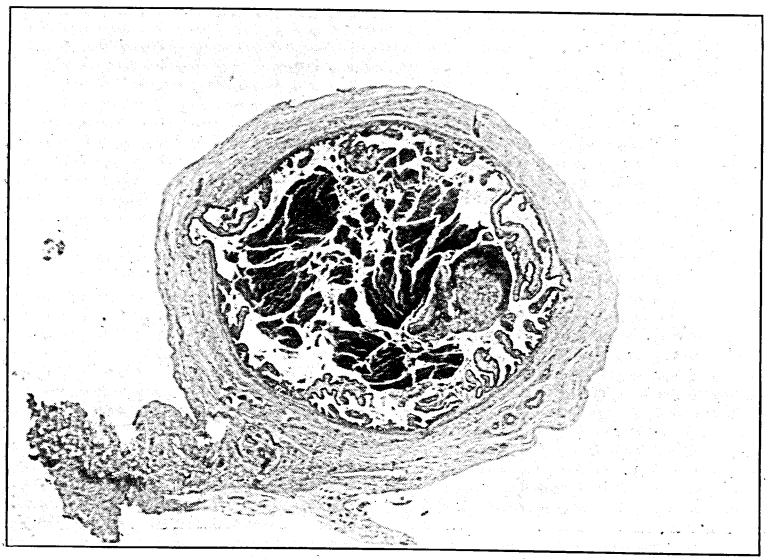

Fig. 14. Purulent Salpingitis, Case 2

Low-power section of uterine tube. Note the purulent exudate in the lumen.

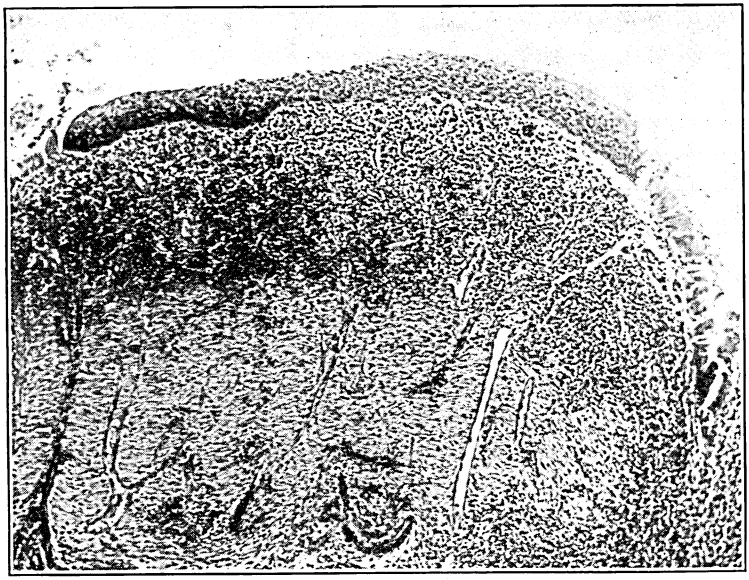

Fig. 15. Section Through Caruncula, Case 7

Note great thickening of uterine epithelium, stratified over caruncula and simple columnar at the border. "Ectodermoisering."

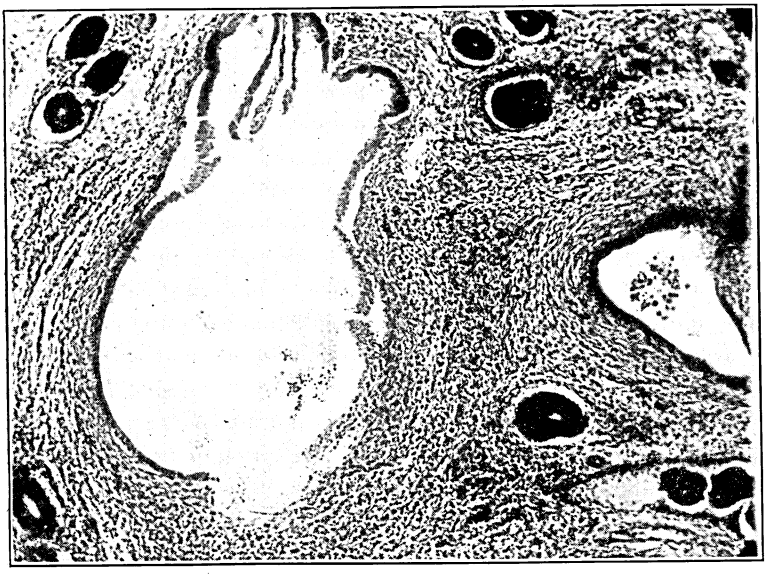

Fig. 16. Dilated Uterine Glands, Case 2

There is considerable destruction of the glandular epithelium. Other deeply stained glands in same section remain normal.

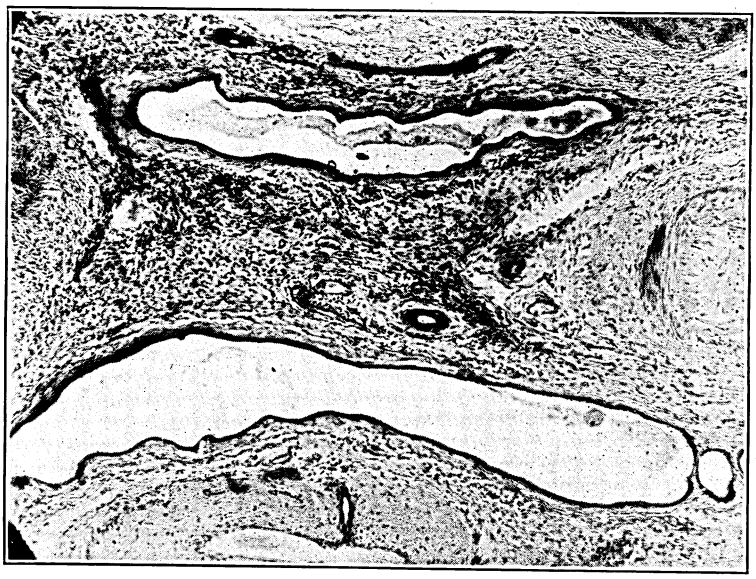

Fig. 17. Section Through Wall of Uterus, Case 7

Note fibrosis of uterine stroma, dilation of uterine glands and atrophy of glandular epithelium.

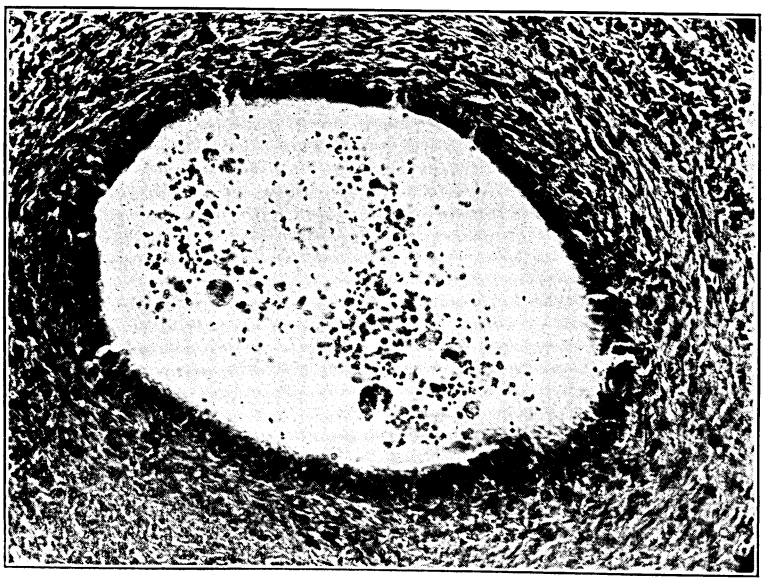

Fig. 18. Section Through Dilated Uterine Gland, Case 2

Note connective tissue proliferation surrounding gland and exudate in its lumen, mostly polymorphonuclears.

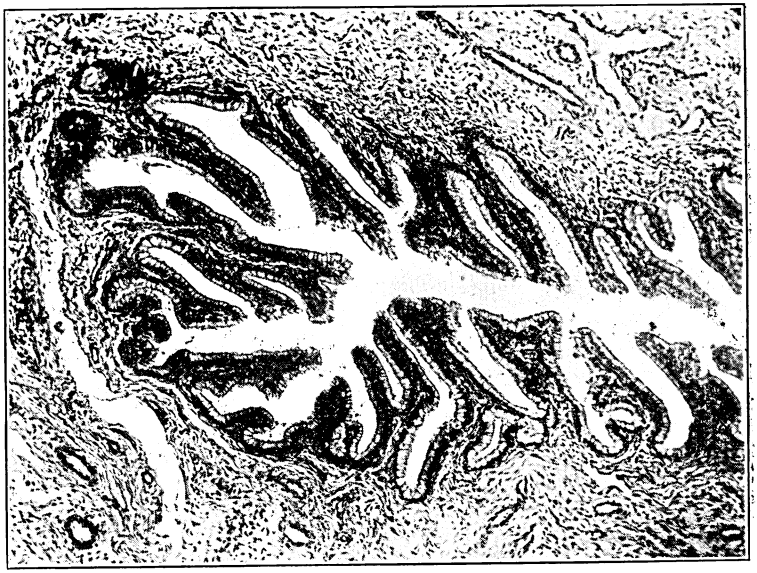

Fig. 19. Normal Fold in *Cervix Uteri*, Case 5

These folds may harbor pathogenic bacteria. In them infection is persistent when once started.

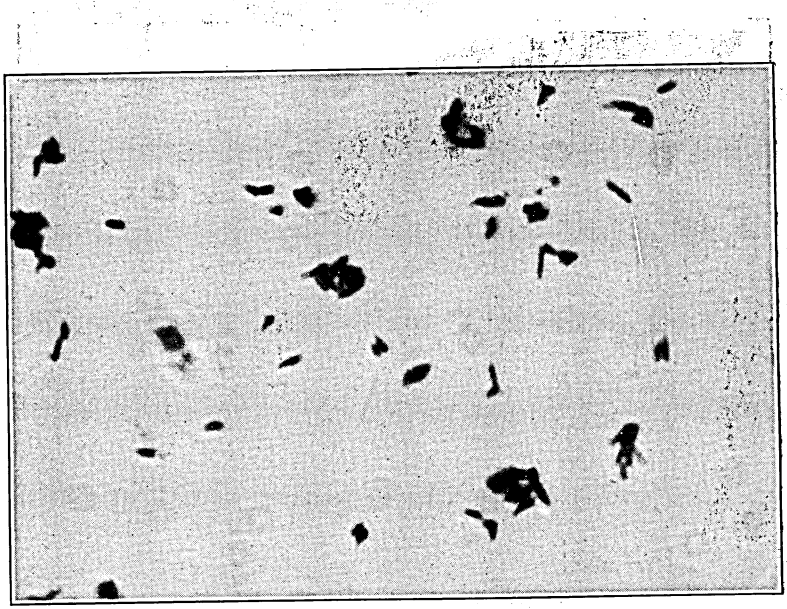

Fig. 20. *B. pyogenes*, Case 18

Note the characteristic clusters, parallel grouping and diphtheroid types.

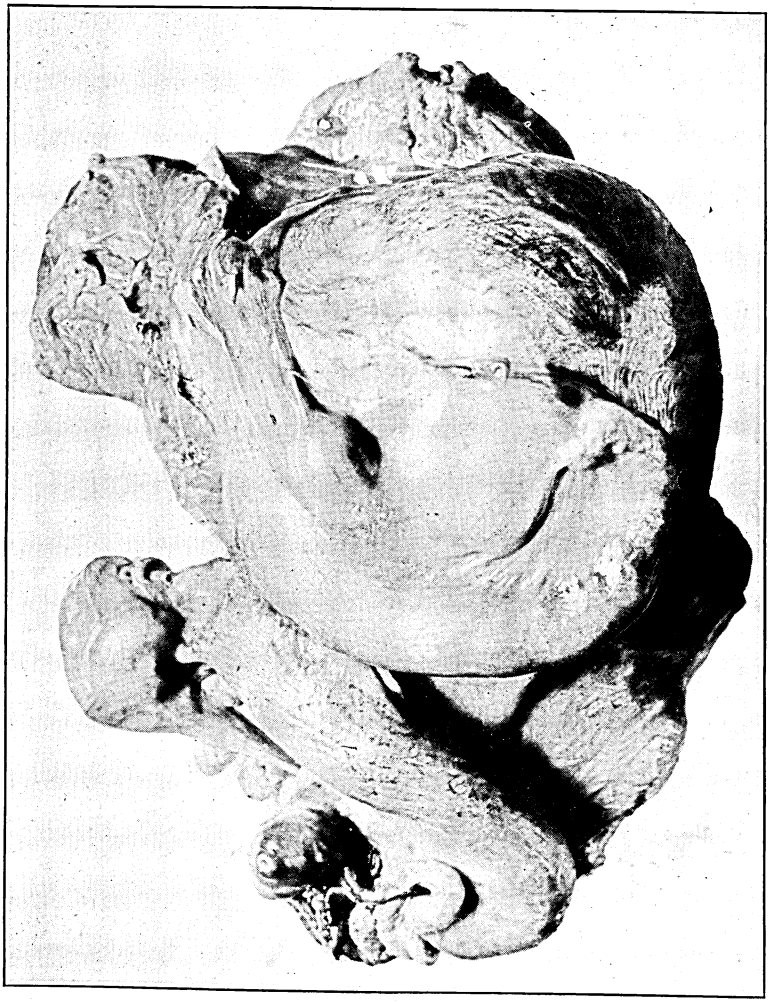

Fig. 21. Gross specimen, Genitalia, Case 4
Shows extensive periuterine abscesses.

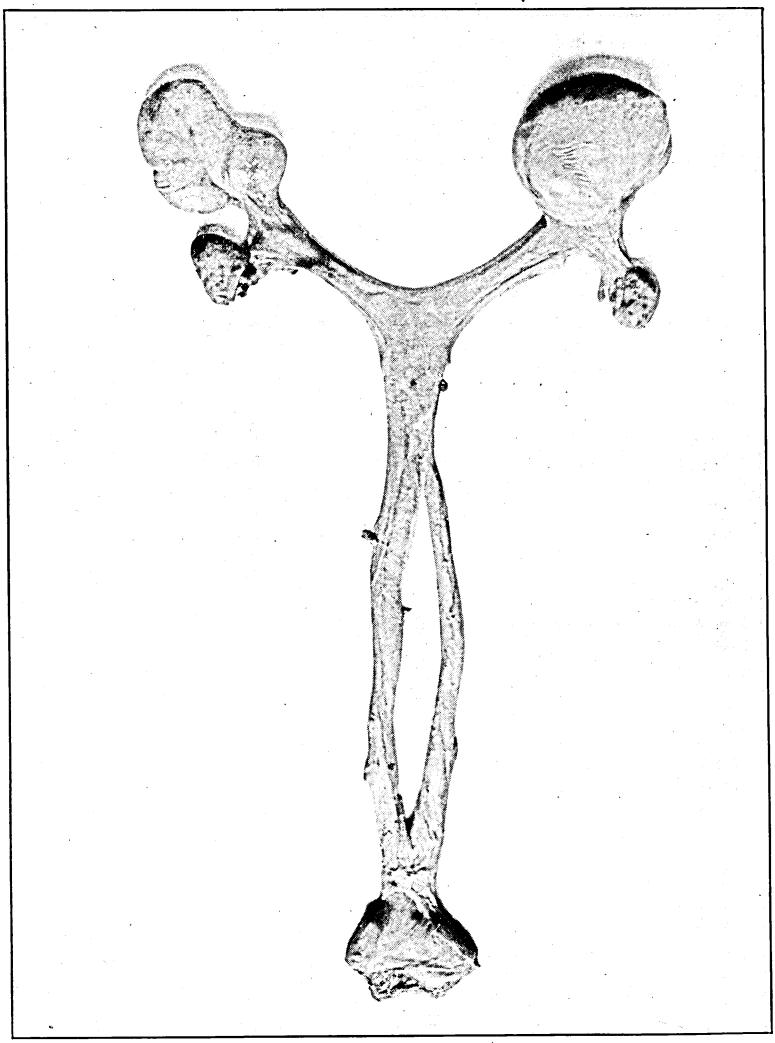

Fig. 22. Maldeveloped Genitalia, Case 13